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TRYPARSAMIDE IN THE TREATMENT OF NEUROSYPHILIS: A STUDY BASED ON OBSERVATION OF 152 PATIENTS FOR EIGHTEEN MONTHS *

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To those who find themselves obliged to combat daily the obstinacies of neurosyphilis as a therapeutic problem, the development of a new and promising approach must always be welcome. Such an approach and such promise is found in the drug tryparsamide, N-phenylglycinamide-para-arsonic acid, prepared by Jacobs and Heidelberger [1] of the Rockefeller Institute, and suggested as suitable for the treatment of certain aspects of syphilis, especially of the nervous system, by Brown.[2] At the hands, first, of Lorenz, Loevenhart, Bleckwenn and Hodges,[3] and subsequently of Moore, Robinson and Keidel,[4] this com-

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1. Jacobs, W. A., and Heidelberger, M.: Aromatic Arsenic Compounds, Ser. I, II and III, J. Am. Chem. Soc. **41**:1581-1644, 1917. Jacobs, W. A., and Heidelberger, M.: Chemotherapy of Trypanosome and Spirochete Infections. Chemical Series I. *N*-Phenylglycineamine-*p*-Arsonic Acid, J. Exper. Med. **30**: 411-415, 1919.

2. Brown, W. H., and Pearce, Louise: Chemotherapy of Trypanosome and Spirochete Infections, Biol. ser. I, II, III and IV, J. Exper. Med. **30**:417-496, 1919; Brown, W. H., and Pearce, Louise: Therapeutic Action of *N*-Phenylglycineamide-*p*-Arsonic Acid (Tryparsamide) Upon Experimental Infections of Trypanosoma Rhodesiense, ibid. **33**:193-200, 1921; Brown, W. H., and Pearce, Louise: Tryparsamide: Its Action and Use, J. A. M. A. **82**:5-9, 1924.

3. Lorenz, W. F.; Loevenhart, A. S.; Bleckwenn, W. J., and Hodges, F. J.: The Therapeutic Use of Tryparsamide in Neurosyphilis, J. A. M. A. **80**: 1497-1502 (May 26) 1923.

4. Moore, J. E.; Robinson, H. M., and Keidel, A.: Tryparsamide in the Treatment of Syphilis, J. A. M. A. **82**:528-535 (Feb. 16) 1924.

pound has received a carefully controlled clinical trial in the treatment of neurosyphilis, special attention being given to the risk of toxic action on the optic mechanism, which was foreshadowed by Pearce [5] in her use of the drug in the treatment of South African sleeping sickness.

GENERAL RESULTS BY STANDARD METHODS IN NEUROSYPHILIS

It would be unfair to the extended and effective work done in the past decade by syphilologists the world over on the treatment of neurosyphilis with various applications of mercury, the iodids and the arsphenamins, to speak of tryparsamide as if there had never been an effective means of dealing with a considerable portion of cases of neurosyphilis. Effective methods for the treatment of neurosyphilis have been discussed extensively by Swift and Ellis,[6] Fordyce,[7] Gennerich,[8] Sachs,[9] Solomon,[10] and many others. Even without tryparsamide, there are at the present time a variety of technics employing standard drugs, which if early and properly applied, will control and apparently arrest syphilitic lesions of the nervous system that a decade ago were generally accepted as beyond the reach of anything but the resolving power of time and the dispensations of Providence. Stokes and Shaffer,[11] from the Section on Dermatology and Syphilology of the Mayo Clinic, have found that the systematic use of arsphenamin intravenously and, if necessary, intraspinally, with a soluble mercurial salt intramuscularly and sodium iodid intravenously, was capable of producing a practical return of serologic and symptomatic normality in 91 per cent. of cases of meningeal neurosyphilis, 74 per cent. of cerebrospinal neurosyphilis, 48 per cent. of tabetic neurosyphilis and 39

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5. Pearce, Louise: Studies on the Treatment of Human Trypanosomiasis with Tryparsamide. (The Sodium Salt of *N*-Phenylglycineamide-*p*-Arsonic Acid), J. Exper. Med. **34,** Suppl. 1, 1-104, 1921.

6. Swift, H. F., and Ellis, A. W. M.: The Treatment of Syphilitic Affections of the Central Nervous System with Especial Reference to the Use of Intraspinous Injections, Arch. Int. Med. **12**:331-345, 1913. Swift, H. F.: A Study of Serum Salvarsanized in Vitro, J. Exper. Med. **24**:373-386, 1916.

7. Fordyce, J. A.: Results of Treatment in Syphilis of the Nervous System, Brit. J. Dermat. & Syph. **36**:47-63, 1924.

8. Gennerich, W.: Die Syphilis des Zentralnervensystems; ihre Ursachen und Behandlung, Berlin, J. Springer, 1922.

9. Sachs, B.: On the Intravenous, not the Intraspinal, Use of Arsphenamin in Syphilis of the Nervous System, Arch. Neurol. & Psychiat. **1**:277-284 (March) 1919. Truth About Intraspinal Injections in Treatment of Syphilis of the Nervous System, J. A. M. A. **69**:681-683 (Sept. 1) 1917.

10. Solomon, H. C.: The Treatment of Neurosyphilis, J. A. M. A. **81**: 1742-1748, 1923.

11. Stokes, J. H., and Shaffer, L. W.: Results Secured by Standard Methods of Treatment in Four Hundred and Five Cases of Neurosyphilis, to be published.

per cent. of vascular neurosyphilis, these observations applying to 405 patients treated and observed for not less than two years and for an average of three and one-half years. Results such as these have convinced us that we are not helpless in the face of an involvement of the nervous system in the course of syphilis, and that in the examination of the possibilities of a new preparation, we have a basis of comparison. A new drug for the treatment of neurosyphilis must offer something distinctive on one or all of the following counts: clinical and serologic results when other methods have failed, fewer complications and a greater margin of safety than older methods; lessened expense, discomfort, loss of time and inconvenience for the patient, and permanence of results. Tryparsamide can be examined at the present time from the standpoint of the first three points. Only a greater lapse of time than that available in any currently reported investigation can determine the issue of permanence.

TECHNIC AND RATIONALE OF TRYPARSAMIDE TREATMENT IN NEUROSYPHILIS

Before discussing our experience with these various factors, we should direct attention to certain general properties of tryparsamide and to the rationale and technic of its employment. The drug is a white crystalline powder, readily soluble in cold distilled water, and suitable for intravenous administration in 33.3 per cent. aqueous solution. The dose for the adult male ranges, as determined by the experience of Pearce, Lorenz and his associates, and of Moore and his associates, from 1 to 4 gm., with an average of from 2 to 3 gm. Since the drug contains 24.57 per cent. of arsenic, the arsenical content of a single dose is evidently enormous (245 mg. to 737 mg.), which renders the more remarkable the observed rarity of all reputed complications of arsenotherapy which have been collected in a decade of experience with the arsphenamins. Injury to eyesight, made unhappily familiar by early experience with atoxyl and hectin, seems to be the only significant complication to be feared from the therapeutic use of tryparsamide. The absence of immediate and late reactions of other types, the simplicity of preparation of the solution, the ease of administration (syringe technic) and the fact that the patient may be treated on an ambulatory basis without interruption of his personal and business activities, such as is necessary in any intensive regimen for the treatment of neurosyphilis by the older methods, give tryparsamide an immense advantage over anything now available, unless it may be the intramuscular use of sulpharsphenamin.[12]

12. Stokes, J. H., and Behn, C. W.: Serologic and Clinical Results in Syphilis with Sulpharsphenamin Administered Intramuscularly, J. A. M. A. **82**: 242 (July 26) 1924.

The rationale of the action of tryparsamide, so far as it is understood, must be clearly kept in mind by all users of the drug. Tryparsamide, while it is a powerful trypanocide, has relatively little direct spirillicidal action. It is not therefore suited to the treatment of early syphilis, or in fact of syphilis in general, when spirillicidal action is desired. It is in no sense a substitute for the arsphenamins in this field, or even for the relatively spirillicidal bismuth. In primary and secondary syphilis, it has no place. In fact, Moore's experience indicates that it is not adapted to the treatment of early neurosyphilis to the exclusion of the standard drugs, for it neglects the syphilis, so to speak, by its lack of direct action on the organisms. The summary of its action by Brown and Pearce ranks it as a stimulator of resistance and of the defensive mechanism. Voegtlin [13] and his collaborators have shown that it leads a considerable list of arsenical drugs in its ability to penetrate the nervous system, being markedly superior in this respect to the familiar arsphenamin and neo-arsphenamin. The correlation of these factors into an entirely satisfactory explanation of the action of the drug is still scarcely complete. The important point for the physician to remember is that the drug is entirely out of place in the treatment of early syphilis, that it can hardly be regarded as a general remedy for syphilis, and that its chief applications are at present limited to the field of fully established or late neurosyphilis and trypanosomiasis.

The eye complications of treatment by tryparsamide have led the Rockfeller Institute, with commendable caution, to make the drug available only to clinics and institutions that are equipped to administer the drug on a charity basis, which are able to control the serologic and clinical results, and to assume responsibility for the prevention of eye complications, so far as they are preventable. It is through the courtesy of the Rockefeller Institute that this study of the clinical application of the drug to the treatment of neurosyphilis has been made possible.

METHODS AND MATERIAL OF THIS STUDY

The treatment employed in our cases is intentionally that described by Lorenz, Loevenhart and associates, in order to make comparisons with their results possible and to avoid, furthermore, the interpretative factors of error introduced into estimations of its therapeutic effect by the synchronous or alternate employment of the arsphenamins. These observers administered weekly injections of tryparsamide, usually in 3 gm. doses, in courses ranging from eight to ten weeks, accompanied

13. Voegtlin, C.; Smith, M. I.; Dyer, Helen, and Thompson, J. W.: Penetration of Arsenic into the Cerebrospinal Fluid, with Particular Reference to the Treatment of Protozoal Infections of the Central Nervous System, Pub. Health Rep. **38**:1003-1021, 1923.

by intramuscular injections of mercuric salicylate in 1 grain doses, given during the seven-day interval between the tryparsamide injections. No iodid or arsphenamin was used in our cases, and no treatment was given in the rest intervals of two months between tryparsamide courses. The use of mercury salicylate was believed by Lorenz and his co-workers to increase the permanence of the tryparsamide effect. In our tabulations, the results at the end of one course, two courses, and in some cases, three courses, are given separately.

Our total series comprises 152 patients, forty of whom had been committed to the Rochester State Hospital for the Insane with the diagnosis of paralytic dementia. The remaining 112 patients were under the care of the Section on Dermatology and Syphilology of the Mayo Clinic. Most of these patients had been under our observation and treatment for a number of years, and on many of them the utmost resources of modern treatment had been exhausted without permanent or, in some cases, even temporary results. It will be apparent that in this group, we subjected tryparsamide to a severe test of efficiency, which at once places the results reported in a special class, superior in a sense to the previously reported results of standard methods of treatment. The Mayo Clinic patients were classified in six groups: (1) general paralysis, confirmed by clinical and serologic evidence, and, in many cases, by therapeutic test; (2) previously treated resistant neurosyphilis of the type usually classified as *paresis sine paresi* of Solomon, or asymptomatic paresis of Lorenz, Loevenhart and their associates; (3) tabes dorsalis without gastric crises; (4) tabes dorsalis with gastric crises; (5) neurosyphilis associated with heredosyphilis, including five cases of juvenile paresis and one of tabetic gastric crises, and (6) five cases of multiple sclerosis and one of erythema induratum.

It should be pointed out with reference to the group of cases spoken of as *paresis sine paresi* that we have not been inclined to accept a diagnosis of clinical paresis simply on the score of first zone colloidal gold or colloidal benzoin tests on the earlier examinations of the spinal fluid. We have felt that a therapeutic test by standard methods of treatment should have failed to accomplish the arrest of the process before we attached the more or less stigmatizing and discouraging term "paresis" to the diagnosis. For this reason, our results with tryparsamide in the asymptomatic group with serologic signs of paresis, although good, are less striking than those of certain other observers, because the patients who have responded to ordinary treatment have been eliminated from consideration. That tryparsamide has been able to accomplish so much for the resistant patients is, therefore, a species of "net tribute" and indicates results not on the whole obtainable by

other means. We felt that only those patients who had had a trial of ordinary methods without result should be asked to assume the possible risk to eyesight involved in the use of tryparsamide.

With reference to our serologic methods, two factors of interpretative importance must be noted. The Wassermann technic employed on both blood and spinal fluid, in the more recent examinations (since June, 1923), has been that of Kolmer. It has been our experience that this technic is more sensitive, and that positive reactions persist longer under all forms of treatment than with the majority of Wassermann technics. It is therefore distinctly more of an achievement to obtain and hold a negative quantitative Kolmer Wassermann reaction on spinal fluid or blood than a negative Wassermann reaction by other technics with which we are familiar. On the other hand, it may be that the difficulty experienced by Moore and his co-workers in reversing blood Wassermann reactions with tryparsamide may be due to a difference in Wassermann technic, or possibly to the fact that they did not use mercury synchronously, as did Lorenz and Loevenhart, and we ourselves.

RESULTS IN ADVANCED PARALYSIS (HOSPITAL CASES)

Findings in a group of forty paretic patients who had been committed to state hospital care are summarized in Table 1. It should be noted that this group is divided into two on the basis of spinal fluid findings. Patients with the clinical picture of paralysis and strongly positive blood and spinal fluid Wassermann reactions were separated from the patients with apparently more advanced and serious types of the disease and those whose blood Wassermann reactions were positive and spinal fluids negative. The question may well be raised as to whether these patients, in spite of their negative spinal fluids, should be considered as having paresis. We have been inclined to speak of them as having "vascular paresis," as the negative spinal fluid has, in our experience, been most frequently associated with the vascular types of cerebral lesions.

It is apparent that the outlook for clinical improvement in advanced or fully developed cases of paresis which have crossed the line of a mental deterioration so marked as to cause commitment to an institution, is relatively poor. This is, of course, obvious, for restoration of degeneration in the nervous system is more than should be expected of any drug. In our observations of these patients committed to an institution, we were impressed by the occurrence of transient improvement under tryparsamide, followed shortly by a markedly accelerated decline until death supervened. The course of the markedly advanced case may, therefore, sometimes be shortened rather than prolonged by

TABLE 1.—*Results of Treatment in Forty Institutional Patients with Advanced Paresis*

		Clinical Result			Blood Wassermann Reaction					Cerebrospinal Fluid												
										Wassermann Reaction				Globulin			Cells			Colloidal-benzoin		
Parenchymatous Paralysis	Total	Good	Fair	Unimproved	Reversed	Reduced	Always negative	Always positive	Increased	Negative	Reduced	Unchanged	Increased	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged
Patients	24	4	2	18	6	6	2	5	5	2	16	5	1	2	1	21	12	12	..	1	21	2
Percentage	..	16	8	76	25	25	8	20	20	8	66	20	4	8	4	88	50	50	..	4	88	8
Patients	23	3	3	17	11	5	2	5	..	3	16	4	..	7	1	15	23	..	..	9	13	1
Percentage	..	13	13	74	48	21	8	21	..	13	70	17	..	30	4	65	100	..	..	39	56	4
Three deaths																						
"Vascular" Paralysis																						
Patients	9	1	1	7	2	3	1	3	..	1	2	6	..	3	1	5	9	..	..	3	5	1
Percentage	..	11	11	77	22	33	11	33	..	11	22	66	..	33	11	55	100	..	..	33	55	11
Patients	5	1	1	3	2	1	..	1	1	5	..	..	..	2	1	2	4	1	..	3	1	1
Percentage	..	20	20	60	40	20	..	20	20	100	..	..	..	40	20	40	80	20	..	60	20	20
Eleven deaths																						

Parenchymatous Paralysis	Treatment
Patients	Ten injections of tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain (0.06 gm.) each, intramuscularly
Percentage	
Patients	Twenty injections of tryparsamide, 3 gm. each, intravenously, and twenty injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	
Three deaths	
"Vascular" Paralysis	
Patients	Ten injections of tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	
Patients	Twenty injections of tryparsamide, 3 gm. each, intravenously, and twenty injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	
Eleven deaths	

TABLE 2.—*Results of Treatment of Thirty-One Patients (Not Institutional) With Early Paresis*

		Clinical Result			Blood Wassermann Reaction						Cerebrospinal Fluid													
											Wassermann Reaction				Globulin			Cells			Colloidal-benzoin			
Group 1 Paralysis	Total	Good	Fair	Unimproved	Reversed	Reduced	Always negative	Always positive	Increased	Blood Not Examined	Negative	Reduced	Unchanged	Increased	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Spinal Fluid Not Examined
Patients	31	17	9	5	1	1	1	22	0	6	0	17	10	2	3	0	26	24	5	0	7	16	6	2
Percentage	..	55	29	16	3	3	3	71	..	19	..	55	32	6	9	..	84	77	16	..	22	50	19	6
After second course:																								
Patients	21	14	4	3	4	1	1	9	0	6	2	13	4	0	4	4	11	15	4	0	10	6	3	2
Percentage	..	66	19	14	19	5	5	42	0	29	10	61	20	0	20	20	51	71	20	0	48	29	14	9
After third course:																								
Patients	6	5	1	..	1	..	..	2	..	3	1	4	1	..	2	1	3	6	..	..	3	2	1	..
Percentage	..	83	16	..	16	..	..	33	..	50	16	66	16	..	33	16	50	100	..	..	50	33	16	..

Group 1 Paralysis	Treatment
Patients	Ten injections tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	
After second course:	
Patients	Twenty injections tryparsamide, 3 gm. each, intravenously, and twenty injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	
After third course:	
Patients	Thirty injections tryparsamide, 3 gm. each, intravenously, and thirty injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	

treatment, a fact not unfamiliar to those who have used arsphenamin intensively for such patients.

RESULTS IN EARLY CLINICAL PARESIS

Table 2 presents the results of tryparsamide treatment of patients whose condition in general was much less advanced than of those in the institutional group. While there were occasional patients with definite deteriorations, the majority were either in the early hyperirritable or mildly demented phases with grandiose ideas, tremor, slight fogging of consciousness and disorientation, and occasional persecutory delusions. The symptomatic response of some of these patients, who had, as in Case 9, received the utmost that the standard forms of treatment could offer, was a most convincing tribute to the immediate efficiency of tryparsamide. A relatively small proportion received no benefit, and an occasional case progressed. We saw no evidence in this small group of a tendency to precipitate unfavorable accidents or to hasten the decline of the patient, as among those with late paresis.

It is thus apparent that clinical results outstrip the serologic response of both blood and spinal fluid in this group of cases. The most prompt response is that of the cell count, which was reduced to normal in all cases by the end of the third course. The next abnormality to respond is the first zone colloidal benzoin reaction, which rapidly loses its paretic characteristics. In fact, in this early effect on the colloidal reactions there may ultimately appear a clue to the action of the drug as distinguished from the much slower response of patients under other forms of treatment. It should be noted that the colloidal gold reaction is more sensitive than colloidal benzoin, and persists longer. The tendency for all reactions to return to normal and to increase with the continuance of treatment seems to be definite, so that there is reason to hope that sufficiently prolonged treatment will bring about a complete reversal of all abnormal findings.

RESULTS IN ASYMPTOMATIC PARALYSIS (PRE-PARALYSIS OR PARESIS SINE PARESI)

In Table 3 are the results of treatment with tryparsamide of patients who had been given intensive standard treatment. The asymptomatic paralysis group of Lorenz and Loevenhart and our own classification of *paresis sine paresi* are included in the table. In this group, the clinical symptoms are not marked, or may be entirely absent, so that it is easy to obtain, with the first course, a high percentage of clinical improvement. Some of the most interesting observations on the effect of tryparsamide were recorded; for example, its effect on the intelligence and alertness of patients who had appeared fairly normal; great

TABLE 3.—*Results with Tryparsamide in Forty-Three Previously Treated Patients With Neurosyphilis, Including Paresis Sine Paresi*

		Clinical Result			Blood Wassermann Reaction						Cerebrospinal Fluid												
											Wassermann Reaction				Globulin			Cells			Colloidal-benzoin			
Group 2 Neurosyphilis with Much Previous Treatment	Total	Good	Fair	Unimproved	Reversed	Reduced	Always negative	Always positive	Increased	Blood Not Examined	Negative	Reduced	Unchanged	Increased	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Spinal Fluid Not Examined
Patients	43	35	4	4	5	2	18	2	4	12	2	15	17	4	9	3	26	26	8	4	6	16	16	5
Percentage	..	82	9	9	11	5	42	5	9	27	5	35	39	9	20	7	60	60	18	9	14	37	37	11
Patients	24	16	4	4	5	0	12	1	2	4	3	13	3	4	3	3	17	17	4	2	3	11	9	1
Percentage	..	66	17	17	20	0	50	4	8	17	12	54	12	17	12	12	70	70	17	8	12	46	37	4
Patients	4	2	2	0	0	0	3	0	0	1	1	1	2	0	1	0	3	4	0	0	1	3	0	0
Percentage	..	50	50	0	0	0	75	0	0	25	25	25	50	0	25	0	75	100	0	0	25	75	0	0

Treatment
Ten to twelve injections tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly
Twenty injections tryparsamide, 3 gm. each, intravenously, and twenty injections mercuric salicylate, 1 grain each, intramuscularly
Thirty injections tryparsamide, 3 gm. each, intravenously, and thirty injections mercuric salicylate, 1 grain each, intramuscularly

TABLE 4.—*Results of Treatment of Resistant Tabes With or Without Gastric Crises*

		Clinical Result			Blood Wassermann Reaction						Cerebrospinal Fluid												
											Wassermann Reaction				Globulin			Cells			Colloidal-benzoin			
Group 3 Tabes Dorsalis without Gastric Crises	Total	Arrest	Improved	Unimproved	Reversed	Reduced	Always negative	Always positive	Increased	Blood Not Examined	Negative	Reduced	Unchanged	Increased	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Spinal Fluid Not Examined
Patients	7	4	2	1	1	0	1	0	0	5	1	3	2	0	1	1	4	4	1	1	2	2	2	1
Percentage	..	57	30	14	14	0	14	0	0	71	14	43	30	0	14	14	57	57	14	14	30	30	30	14
Patients	5	3	2	0	2	0	1	0	1	1	0	4	0	0	2	1	1	4	0	0	3	1	0	1
Percentage	..	60	40	0	40	0	20	0	20	20	0	80	0	0	40	20	20	80	0	0	60	20	0	20
Lorenz et al. tabes	5	4	1	0	100	..	..	..	..	..	40	60	..	..	40	60	..	80	20	..	20	80	..	..
Group 4 Tabes Dorsalis with Gastric Crises																								
Patients	8	5	2	1	..	..	..	..	..	6	..	1	..	..	..	..	1	1	..	..	..	..	1	7
Percentage	..	62	25	12	..	..	..	..	..	75	..	12	..	..	..	..	12	12	..	..	..	..	12	87

Treatment
Ten injections tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly
Twenty injections tryparsamide, 3 gm. each, intravenously, and twenty injections mercuric salicylate, 1 grain each, intramuscularly
Ten injections tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly

increase in working capacity; a feeling as if a cloud were lifting from the mind and markedly improved appetite and sexual activity in several cases. Of one patient who had an early persecutory delusion with insight, it was repeatedly noted that the delusion would become more accentuated between treatments or on the employment of arsphenamin, which was occasionally administered, but that the delusion disappeared in almost quantitative fashion after each injection of tryparsamide.

The effect of two courses of treatment on the blood Wassermann reaction in this group of cases is not striking. The effect on the spinal fluid reaction is better, but on the whole not strikingly superior to that secured in cases of more outspoken paralysis. It is, of course, scarcely fair to rate the serologic efficiency of the drug on the basis of two, or even three, courses of treatment, as one would hardly be inclined to expect markedly better results from other methods. It is certainly suggested that new therapeutic combinations of tryparsamide with other drugs, including perhaps the iodids, bismuth and sulpharsphenamin, should be tried in the effort to reinforce its undoubtedly great symptomatic value with a more active effect on the serology.

In the use of tryparsamide in these two groups of cases, we witness at its maximum, perhaps, the dissociation of serologic and symptomatic results. The almost miraculous transformations of the mental state of paralysis which tryparsamide can produce may at times be wholly dissociated for considerable periods from any signs of improvement in the Wassermann reaction on either blood or spinal fluid. On the other hand, the response of the meningeal phase is much more prompt, and some of our patients have been willing to make wagers on a drop in their cell counts, even after a relapse, on the basis of changes in their symptoms which they could detect.

RESULTS IN TABES WITH AND WITHOUT GASTRIC CRISES

Our use of tryparsamide in the attack on the most resistant phases of neurosyphilis has, of course, led us, as in the case of other investigators, to devote ourselves mainly to the treatment of paresis and preparesis. We have, however, a few examples of resistent tabes treated with tryparsamide (Table 4), which include seven cases of patients without gastric crises and eight with gastric crises. It is apparent, considering the fact that previous treatment had failed to improve the condition of these patients, that the effect of tryparsamide is good, and that it deserves a trial under suitable control. Certain of the results in gastric crises, as, for example, in Case 6, were remarkable and justify further trial of the drug in this condition in particular. All the patients with crises had negative spinal fluid findings; thus there is no serologic phase in this group.

TABLE 5.—Results of Treatment in Six Cases of Neurosyphilis, Five Patients With Tabetic Forms and One Patient With Gastric Crises

TABLE 5.—*Results of Treatment in Six Cases of Heredosyphilis: Five Patients With Juvenile Paresis and One Patient With Gastric Crises*

Group 5 Heredosyphilis with Neurosyphilitic Involvement	Total	Clinical Result: Good	Fair	Unimproved	Blood Wassermann Reaction: Reversed	Reduced	Always negative	Always positive	Increased	Blood Not Examined	Cerebrospinal Fluid: Wassermann Reaction: Negative	Reduced	Unchanged	Increased	Globulin: Negative	Reduced	Unchanged	Cells: Negative	Reduced	Unchanged	Colloidal-benzoin: Negative	Reduced	Unchanged	Spinal Fluid Not Examined	Treatment
Patients	6	1	4	1	0	0	0	5	0	1	0	2	3	0	2	1	3	4	1	0	3	2	0	1	Ten injections tryparsamide, 2 gm. each, intravenously, and ten injections mercuric salicylate, 0.5 grain each, intramuscularly
Percentage	..	16	66	16	0	0	0	83	0	16	0	33	50	0	33	16	33	66	16	0	50	33	0	16	
Patients	3	1	2	0	0	0	0	3	0	0	0	1	1	1	0	1	2	2	1	0	3	0	0	0	Twenty injections tryparsamide, 2 gm. each, intravenously, and twenty injections mercuric salicylate, 0.5 grain each, intramuscularly
Percentage	..	33	66	0	0	0	0	100	0	0	0	33	33	33	0	33	66	66	33	0	100	0	0	0	

TABLE 6.—*A Comparison of Results in Late Institutional Patients With Late Paresis and Noninstitutional Patients With the Results of Lorenz, Loevenhart, Bleckwenn and Hodges*

Late Paralysis	Total	Clinical Result: Arrest	Improved	Unimproved	Blood Wassermann Reaction: Reversed	Reduced	Always negative	Always positive	Increased	Blood Not Examined	Cerebrospinal Fluid: Wassermann Reaction: Negative	Reduced	Unchanged	Increased	Globulin: Negative	Reduced	Unchanged	Cells: Negative	Reduced	Unchanged	Colloidal-benzoin: Negative	Reduced	Unchanged	Spinal Fluid Not Examined	Treatment
Patients	24	4	2	18	6	6	2	5	5	..	2	16	5	1	2	1	21	12	12	0	1	21	2	..	Ten injections tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	..	16	8	76	25	25	8	20	20	..	8	66	20	4	8	4	88	50	50	0	4	88	8	..	
Patients	23	3	3	17	11	5	2	5	0	..	3	16	4	0	7	1	15	23	0	0	9	13	1	..	Twenty injections tryparsamide, 3 gm. each, intravenously, and twenty injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	..	13	13	74	48	21	8	21	0	..	13	70	17	0	31	4	65	100	0	0	39	56	4	..	
Lorenz et al. Late Paralysis																									
Patients	42	21	4	17	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
Percentage	..	50	9	41	80	17	3	..	..	..	30	54	16	..	34	52	14	50	50	..	12	48	40	..	
Paralysis																									
Patients	31	17	9	5	1	1	1	22	..	6	..	17	10	2	3	..	26	24	5	..	7	16	6	2	Ten injections tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	..	55	29	16	3	3	3	71	..	19	..	55	32	6	9	..	84	77	16	..	22	50	19	7	
Patients	21	14	4	3	4	1	1	9	..	6	2	13	4	..	4	4	11	15	4	..	10	6	3	2	Twenty injections tryparsamide, 3 gm. each, intravenously, and twenty injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	..	67	19	14	19	5	5	42	..	29	10	61	20	..	20	20	51	71	20	..	48	29	14	9	
Lorenz et al. Early Paralysis																									
Patients	12	7	5	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
Percentage	..	60	40	..	84	16	..	..	..	..	40	52	8	..	56	44	..	72	28	..	24	68	8	..	

Our series includes further five cases of juvenile paralysis of the heredosyphilitic type, and a heredosyphilitic boy with tabetic gastric crises (Table 5). In these paralytic children, the clinical improvement could be rated as about 20 per cent. following one course of tryparsamide. This is obviously not a fair trial of the ultimate efficiency of the drug.

COMPARISON OF RESULTS WITH THOSE OF OTHER INVESTIGATORS

Tables 6 and 7 compare our results with those published by Lorenz and Loevenhart and their associates, and by Moore, Robinson and Keidel. A comparison with Lorenz and his associates in the treatment of a few tabetic patients is included in Table 5. It is apparent that our clinical results are not quite as good as those reported by Lorenz and by Moore, and their co-workers; 47 per cent. as compared with 62.8 (Lorenz) and 66.6 per cent. (Moore). Part of this discrepancy is explainable on the ground of our briefer experience, which has permitted only two courses to be given to most of our patients. Part of it may also be due to the fact that a large proportion of our patients had, for a period of months or years, been subjected to the most determined modern treatment, with the arrest and restoration of all those with more treatable disease and the development of a residue of intractable disease which, as we have said, constituted the most severe test to which we could put the new drug. Under the circumstances, we do not doubt that, aside from complications, tryparsamide is a most important instrument in the treatment of resistant neurosyphilis.

Serologically we agree with Lorenz, Loevenhart and their associates on the reversal of the blood Wassermann reaction, and we secured markedly better results than Moore and his co-workers. Part of this result, as I have suggested, may be due to the fact that Moore did not use mercury synchronously. On the spinal fluid Wassermann reaction, our results are definitely less good for complete reversals, because of the great sensitiveness of the quantitative Kolmer test, which in other forms of treatment has shown the same tendency to register slight degrees of positiveness which were negative with ordinary tests. In the reductions of the spinal fluid Wassermann reaction, we secured slightly better results than the foregoing authors, which tends to confirm our explanation. On globulin reduction, a relatively uncertain item, we strike a fair average. In the cell count we have obtained in general better results than either of the authors named. In the colloidal tests, Lorenz and Moore and their associates used colloidal gold, so that the results are hardly directly comparable, but indicate, so far as Moore's and our results are concerned, a fair response.

TABLE 7—*A Comparison of Our Results in Asymptomatic Paresis With the Results of Lorenz, Loevenhart, Bleckween and Hodges. Also a Comparison of Results in Parenchymatous Neurosyphilis With the Results of Both Lorenz et al, and Moore, Robinson and Keidel*

	Clinical Result			Blood Wassermann Reaction						Cerebrospinal Fluid													
										Wassermann Reaction				Globulin			Cells			Colloidal-benzoin			
Asymptomatic Paralysis and Neurosyphilis with Much Treatment	Good	Fair	Unimproved	Reversed	Reduced	Always negative	Always positive	Increased	Blood Not Examined	Negative	Reduced	Unchanged	Increased	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Negative	Reduced	Unchanged	Spinal Fluid Not Examined	Treatment
Patients (43)	35	4	4	5	2	18	2	4	12	2	15	17	4	9	3	26	26	8	4	6	16	16	5	Ten injections tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	82	9	9	11	5	42	5	9	27	5	40	39	9	20	7	60	60	18	9	14	37	37	11	
Patients (24)	16	4	4	5	..	12	1	2	4	3	13	3	4	3	3	17	17	4	2	3	11	9	1	Twenty injections tryparsamide, 3 gm. each, intravenously, and ten injections mercuric salicylate, 1 grain each, intramuscularly
Percentage	66	17	17	20	..	50	4	8	17	12	54	12	17	12	12	70	70	17	8	12	46	37	4	
Lorenz et al. Asymptomatic Paralysis																								
Patients	13	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
Percentage	93	7	..	84	16	..	..	..	..	42	51	7	..	56	44	..	77	23	..	28	72	..	..	
Parenchymatous Neurosyphilis * 78 Patients																								
Percentage	47	18	35	30	9	21	21	5	14	17	59	14	5	23	13	59	81	12	2	36	41	18	5	Twenty injections tryparsamide, 3 gm. each, intravenously, and twenty injections mercuric salicylate, 1 grain each, intramuscularly
Lorenz et al. 78 Patients																								
Percentage	62.8	15.3	21.7	83.3	15.3	..	1.2	..	..	34.6	52.5	12.8	..	42.3	50.0	7.6	68.2	37.1	..	17.9	57.6	24.3	..	
Moore et al. 27 Patients																								
Percentage	66.6	14.8	18.5	6.6	20.0	..	73.3	8.5	..	29.6	51.8	18.5	..	18.5	48.1	33.3	65.0	20.0	15	43.5	26.0	30.4	..	

* (G. P. taboparesis, tabes, paresis sine paresi) S. W.

RESULTS IN NONSYPHILITIC CONDITIONS

Since the foregoing experience, we have used tryparsamide in five cases of multiple sclerosis with as yet no striking result beyond the patient's increased sense of well-being. In fact, the results with tryparsamide in these cases impress us as distinctly inferior to those obtained with arsphenamin. In a case of erythema induratum, no good effect was observed.

MISCELLANEOUS RESPONSES AND REACTIONS

Among miscellaneous observations the following are of interest: Tryparsamide produces a definite symptomatic Herxheimer reaction of a rather tardive type, which resembles that produced by all intensive treatment of syphilis of the nervous system. Patients who are mildly confused at the outset, or slightly hyperirritable, may become almost vegetative on the one hand, or actually maniacal on the other, during the second, third, fourth and fifth weeks of a course of six injections. This matter has been of much practical importance in our work, and precautions against suicide, temporary sequestration with special nursing and even restraint, have been necessary for patients who began treatment in fair condition, who have subsequently done very well, and have been placed in definite remission. A picture, not unlike the hyperirritability seen with overintensive arsenical treatment of patients who do not have neurosyphilis, may occur, and a patient who has shown no signs of mental disturbance may become, in the first two or three weeks, emotional, nervous, and even seem to be threatened with a nervous breakdown. After this period, the recovery is rapid, and the stimulating and supportive effect of the drug gratifying. The effect on the early paretic facies is one of the most interesting. The flabbiness, apathy and the fatuous smile disappear; the lines of the face sharpen; the carriage becomes more erect, the voice clearer and more distinct, and the slurring speech and lip sucking or tremor, disappear. The transformation may be so great as to make it difficult to recognize the patient. There is nothing to compare with these effects in the ordinary treatment of the paretic patient, even though the older forms of treatment may successfully place him in remission. Under tryparsamide treatment, we have repeatedly witnessed the rationalizing of delusions and auditory hallucinations. While the patient may still hear voices, he learns to disregard them as the tryparsamide treatment progresses.

SOCIAL IMPLICATIONS

The social implications of tryparsamide treatment cannot be wholly disregarded by the syphilotherapist. The question as to whether it is possible or permissible to raise a patient from a state of harmless

CASE 1.—*A Man, Aged 29, With Asymptomatic Neurosyphilis, Uninfluenced by Much Previous Treatment, Responded Promptly to Tryparsamide. Note, However, the Meningeal Relapses Under Both Standard and Tryparsamide Treatment. The Slightly Positive Persistent Kolmer Wassermann Reaction on the Fluid Has Been Frequently Observed in Our Experience*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid				Clinical Status
					Wassermann Test	Nonne	Cells	Colloidal benzoin	
Infection ? 7/29/22	Elsewhere, arsphenamin	23	9.2 gm.	Negative	+++ with 0.4, 0.6 and 1.0 c.c.	Positive	90 small leukocytes 13 large leukocytes 17 polymorphonuclears	3333003330000000	Feeling of tightness about neck; numbness in limbs
	Mercuric inunctions, pea-sized	200							
	Sodium iodid, intravenously	6							
8/ 9/22 to 10/26/22	Arsphenamin, intravenously	9	3.1 gm.	(K) negative	++ with 0.4 and 0.6 c.c.; +++ with 1.0 c.c.	Positive	8	3333003333000000	Unchanged
	Swift-Ellis-Ogilvie, intraspinal	6	150 c.c. serum						
	Mercuric succinimid, intramuscularly	21	5.25 grains (0.33 gm.)						
	Sodium iodid, intravenously	19	175 gm.						
10/26/22 to 1/23/23	Mercuric inunctions	80	260 gm.	(K) negative	(K) 412 - -	Positive	28	3333002300000000	Same
	Potassium iodid, intravenously	180	12 gm.						
1/27/23 to 5/31/23	Tryparsamide, intravenously	10	19.5 gm.	(K) 44	(K) 41 - - -	Negative	7	0110000000000000	Feels better; heavy feeling in head and neck gone
5/23/23 to 8/ 1/23	Tryparsamide, intravenously	10	27 gm.	(K) 4 -	(K) 2 - - - -	Positive	4	0000001110000000	No pains in head and neck; memory good; excellent
	Mercuric salicylate, intramuscularly	5	5 grains (0.32 gm.)						
10/10/23 to 12/12/23	Tryparsamide, intravenously	10	30 gm.	(K) negative	(K) negative	Positive	32	0000000310000000	Recurrence of pain in head and neck disappeared after first tryparsamide; feeling fine
	Mercuric salicylate, intramuscularly	5	5 grains (0.32 gm.)	(K) negative	(K) 221 - -	Negative	2	0000000200000000	
1/10/24 to 5/ 7/24	Sulpharsphenamin	5	2 gm.	.....	(K) 4 - - - -	Positive	3 poly. 14	0000003330000000	Feeling fine
	Swift-Ellis-Ogilvie, intraspinal	5	125 c.c. serum						

CASE 2.—*A Man, Aged 45, Showed Marked Improvement on Ordinary Treatment and Serologic Relapses in Response to Tryparsamide as Standard Treatment; Five Years' Observation*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid: Wassermann Test	Cerebrospinal Fluid: Nonne	Cerebrospinal Fluid: Cells	Cerebrospinal Fluid: Colloidal-benzoin	Clinical Status
Infection ?									
3/25/19 to 5/ 3/19	Arsphenamin, intravenously	6	2.3 gm.	Negative	+++ with 0.3 and 0.4 c.c.	Positive	48	0012210000	Inability to control legs; loss of sexual power; slight ataxia; improved
	Mercuric succinimid, intramuscularly	21	5 grains (0.32 gm.)	Negative	+++ with 0.3 and 0.4 c.c.	Positive	25	0043211000	
5/ 3/19 to 8/26/19	Mercuric inunctions	50	100 gm.	Negative	+++ with 0.3 and 0.4 c.c.	Positive	38	1223220000	Sexual power normal; can control legs
8/26/19 to 9/30/19	Arsphenamin, intravenously	6	2.5 gm.	Negative	+++ with 0.3 and 0.4 c.c.	Negative	46	1123310000	Feels fine
11/10/19 to 12/22/19	Arsphenamin, intravenously	4	1.6 gm.	Negative	Negative with 0.3 and 0.4 c.c.	Negative	6	.....	Feels fine, walks normally; does not etagger
	Mercuric succinimid, intramuscularly	16	3 grains (0.19 gm.)						
	Swift-Ellis-Ogilvie, intraspinal	4	100 c.c. serum						
12/22/19 to 5/ 6/20	Mercuric inunctions	40	80 gm.	Negative	Negative with 0.3 and 0.4 c.c.	Negative	2	.....	Feels better than in years
5/ 6/20 to 11/ 2/20	Mercuric inunctions	40	80 gm.	Negative	Negative with 0.3 and 0.4 c.c. (+++ with 0.3 and 0.4 c.c. chol. ant.)	Positive	38	.....	Feels fine
11/ 2/20 to 2/ 2/21	Arsphenamin.....	6	2.4 gm.	Negative	Negative with 0.4 and 1 c.c. (+++ with 0.4 and 1 c.c. chol. ant.)	Negative	2	.....	Feels good; no complaint
	Swift-Ellis-Ogilvie, intraspinal	6	150 c.c. serum						
	Mercuric inunctions	20	40 gm.						
2/ 2/21 to 6/ 1/21	Mercuric inunctions	40	80 gm.	Negative	Negative with 0.4 and 1 c.c.	Negative	7	.....	Looks fine; working every day; walk-improved
6/ 1/21 to 9/ 2/21	Arsphenamin.....	4	1.5 gm.	.....	Negative with 0.4 and 1 c.c.	Negative	1	.....	Feels good
	Swift-Ellis-Ogilvie, intraspinal	4	100 c.c. serum						
8/ 2/21 to 4/10/22	Mercuric inunctions	60	120 gm.	Negative	+++ with 0.4, 0.6 and 1 c.c.	Positive	84	0012210000	Stiff neck; appetite good; working every day
4/10/22 to 5/20/22	Arsphenamin.....	1	0.3 gm.	Negative	Negative with 0.4, 0.6 and 1 c.c.	Negative	12	1122000	Sore gums; otherwise well
	Flumerin (205).....	11	2.2 gm.						
	Mercuric succinimid	4	1 grain (0.06 gm.)						
5/20/22 to 9/18/22	Mercuric inunctions	45	90 gm.	Negative	Negative with 0.4, 0.6 and 1 c.c.	Negative	4	000000000000000	Feels good; "rub" arthritis
9/18/22 to 1/16/23	Mercuric inunctions	60	120 gm.	(K) 21 - - -	(K) 444 - -	Positive	14	.....	Working regularly
1/16/23 to 2/16/23	Arsphenamin.....	2	0.6 gm.	.....	(K) 44 - - -	Negative	17	000003330000000	No complaints
	Swift-Ellis-Ogilvie, intraspinal	2	50 c.c. serum						
2/16/23 to 4/30/23	Tryparsamide.....	10	22.5 gm.	(K) negative	(K) 2 - - - -	Negative	1	000000000000000	General appearance fine
	Mercuric salicylate	4	6 grains (0.4 gm.)						
4/30/23 to 7/ 4/23	No treatment.....	...	.....	(K) 41	(K) 43 - - -	Negative	2	000000000000000	Feels and looks fine
7/ 4/23 to 9/ 9/23	Tryparsamide.....	10	29 gm.	.....	(K) 2 - - - -	Negative	1	000000010000000	Feels fine
	Mercuric salicylate	8	8 grains (0.52 gm.)						
9/10/23 to 11/20/23	No treatment.....	...	.....	.....	(K) negative	Negative	1	000000000000000	Working every day; feels fine
11/21/23 to 4/ 8/24	No treatment.....	...	.....	(K) negative	(K) 4	Negative	1	000000000000000	

CASE 3.—*A Woman, Aged 37, Showed the Good Effect of Tryparsamide in a Patient Who Once Relapsed Under Ordinary Treatment and Who Refused Intraspinal Therapy*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid				Clinical Status
					Wassermann Test	Nonne	Cells	Colloidal-benzoin	
Infection ? to 2/4/22	Mercuric salicylate	12	12 grains (0.78 gm.)	Negative	Negative with 0.4, 0.6 and 1 c.c.	Positive	43	5555543100	Generalized pains; asthenia; partial blindness
2/ 4/22 to 4/ 8/22	Arsphenamin.....	16	7.8 gm.	Negative	Negative with 0.4, 0.6 and 1 c.c.	Negative	8	1233310000	Feels better
	Mercuric succinimid	35	9 grains (0.6 gm.)						
	Sodium iodid, intravenously	23	410 gm.						
4/ 8/22 to 12/11/22	No treatment.....	...	.....	Negative	+++ with 0.4 0.6 and 1 c.c.	Positive	37	000000333200000	No complaints
1/ 2/23 to 2/ 7/23	Arsphenamin.....	11	5.8 gm.	(K) negative	(K) 44 - - -	Positive	9	.....	Feels fine
	Mercuric succinimid	17	3 grains (0.1 gm.)						
	Sodium iodid, intravenously	19	172.5 gm.						
2/ 8/23 to 4/26/23	No treatment.....	...	.....	(K) negative	.....	.....	..	.....	Spell of dizziness; nervous instability
4/27/23 to 7/16/23	Tryparsamide.....	10	27.5 gm.	.....	.....	.....	..	.....	Looks and acts much better
	Mercuric salicylate	7	7 grains (0.4 gm.)						
7/17/23 to 10/13/23	No treatment.....	...	.....	.....	.....	.....	..	.....	Arthritis of hands
10/14/23 to 12/15/23	Tryparsamide.....	9	25 gm.	.....	(K) negative	Negative	2	000000132100000	Much better
	Mercuric salicylate	8	8 grains (0.5 gm.)						
12/16/23 to 3/ 7/24	No treatment.....	...	.....	(K) negative	(K) negative	Negative	2	000000133200000	Feels very well

imbecility and vegetative decline to a partial remisson in which he may be released from custodial care, only to make trouble for his family or to develop sudden explosions of violence, must be weighed and answered for each case. We have seen a patient who was a mere harmless occupant of the corner by the kitchen stove raised by a course of tryparsamide treatment, for the time being, to a roamer, a meddler and a quarrelsome, malicious and intractable person, who greatly hampered his wife's efforts to support the family. There is also room for questioning the value of stimulating the sexual powers of paretic or preparetic patients, as has occurred in several of our cases, in view of the familial disharmony and possible unsocial consequences which may ensue. All these contingencies should be discussed and provided for in talking with the persons responsible for a given patient.

We have watched our cases closely for that rather discouraging earmark of genuine preparesis, the meningeal relapse, which we have observed several times, as illustrated in Cases 1 and 4. The ultimate controllability of this tendency to relapse under treatment with tryparsmide can of course only be determined by further treatment and observation.

We believe, then, that from the foregoing observations we can rate tryparsamide as a highly valuable addition to the treatment of neurosyphilis. On the score of efficiency, we have seen it produce clinical and serologic results in a certain number of cases in which other methods have failed. The symptomatic results are especially remarkable and indeed unique. The drug should be inexpensive; the technic of its administration is simple; it reduces inconvenience, discomfort and economic incapacity for the patient to a minimum. The question of permanence of good effects cannot be decided by any study thus far published. It becomes necessary now to state our experience with the one complication that has threatened to limit the usefulness of this most valuable drug, namely, its effect on eyesight. The experience gained in our series of cases has been summarized from the ophthalmologic standpoint by Lillie; we shall therefore only give in a general way the reactions which may be expected, and discuss the possibility of their control.

INJURY TO EYESIGHT AS A COMPLICATION

Injury to vision by tryparsamide may be discussed under the headings of subjective symptoms and objectively detectable damage. One or the other type of reaction occurred in twelve cases in our series of 152 patients, or an incidence of eight per cent. Of these reactions, four (2.6 per cent.) were subjective in character, and eight (5.4 per cent.) were accompanied by detectable evidence of damage. Like atoxyl, tryp-

CASE 4.—*A Man, Aged 35, Intolerant of Ordinary Treatment, but Much Improved by Tryparsamide, Had Had Repeated Meningeal Relapse. Note, However, the Meningeal Relapse in a Rest Interval Under Tryparsamide*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid				Clinical Status
					Wassermann Test	Nonne	Cells	Colloidal-benzoin	
Infection 1907									
1907 to 6/21/21	Elsewhere: Arsphenamin	13	.....	Negative	+++ with 0.4 and 1 c.c.	Positive	12	.....	Comes for syphilis; lightning pains, nervous
	Intraspinal.....	2							
	Dralnage (spinal)...	5							
	Mercuric salicylate..	30							
	Mercuric inunctions.	30							
6/28/21 to 8/24/21	Arsphenamin.....	8	2.9 gm.	Negative	+ with 0.4 c.c., +++ with 1 c.c.	Positive	10	0455555331	The intraspinal treatment causes severe pains in the leg
	Swift-Ellis-Ogilvie, intraspinal	4	100 c.c. serum						
	Mercuric succinimid	19	4.75 grains (0.3 gm.)						
8/24/21 to 2/ 9/22	Mercuric inunctions	65	130 gm.	Negative	+++ with 0.4, 0.6 and 1 c.c.	Positive	66	5555552100	About the same
2/ 9/22 to 3/28/22	Arsphenamin.....	14	8.1 gm.	Negative	Negative with 0.4 and 1 c.c., ++ with 0.6 c.c.	Positive	3	0233310000	Severe reaction to intraspinal treatment; no change otherwise
	Swift-Ellis-Ogilvie, intraspinal	3	75 c.c. serum						
	Mercuric succinimid	26	8.5 grains (5.5 gm.)						
	Sodium iodid, intravenously	23	250 gm.						
6/27/22 to 8/18/22	Arsphenamin.....	3	0.9 gm.	Negative	+++ with 0.4, 0.6 and 1 c.c.	Positive	15	000000030000000	Feeling better; looks fine
	Flumerin.....	12	2.4 gm.						
	Swift-Ellis-Ogilvie, intraspinal	2	500 c.c. serum		+++ with 0.4, 0.6 and 1 c.c.	Positive	18	001100033000000	
8/18/22 to 4/16/23	Mercuric inunctions	120	400 gm.	(K) 21	(K) 444 - -	Positive	47	003300000000000	Has done more and better work than in years
4/16/23 to 6/20/23	Tryparsamide.....	10	28 gm.	.....	(K) 42 - - -	Positive	6	.....	Upset by overwork; "all shot to pieces"
	Mercuric salicylate..	5	5 grains (0.3 gm.)						
8/27/23 to 10/27/23	Tryparsamide.....	10	29 gm.	(K) negative	(K) 43 - - -	Positive	8	001000033100000	Working hard and in "pink of condition"; feels better than in years
					(K) negative	Positive	5	000000020333200	
12/31/23	....	...	.....	(K) negative	(K) negative	Positive	6	000000033333322	Working hard; feeling fine
3/10/24 to 5/12/24	Tryparsamide.....	5	10 gm.	(K) negative	(K) 4 - - - -	Positive	46 occ. polymorphonuclears	000000333320000	Leg pains and nervous feeling in stomach; looks pale and pudgy
	Sulpharsphenamin..	6	3.2 gm.						
	Mercuric succinimid	14	2.3 grains (0.14 gm.)						
	Sodium iodid, intravenously	8	72.5 gm.	(K) negative	(K) 1 - - - -	Positive	4	000000000000000	

arsamide may give rise to a toxic amblyopia, due perhaps to optic atrophy of retrobulbar origin, and perhaps to central injury, the precise mechanism of whose production is not apparent. This toxic amblyopia may be transient or permanent, and may end in total blindness. Since the lesion is retrobulbar, nothing may be visible in the fundus, even of a patient who has gone totally blind, until some weeks after vision is impaired or lost, when the characteristic pale atrophic disk develops. No patient in our series suffered total loss of sight, although one was permanently reduced to tubular vision.

The first warning that the eyes are being affected usually takes the form of a blurring of vision, especially at the periphery of the field, and a sense as of the encroachment of light waving clouds from the sides and above or below the objects in the direct line of vision. As this is a subjective symptom, one is obliged to rely on the patient for warning that it is developing, and for cooperation in the testing of fields and visual acuity, by which alone the development of organic damage can be recognized. The befuddled and uncooperative paralytic patient cannot, therefore, be relied on to protect himself by calling attention to his symptoms, and the responsible relative must be made to understand clearly the increased risk involved. Other subjective symptoms include a sense of darkening, or of grayness of the visual field, inability to see objects about the feet or at the side, due to contraction of the fields, and light and dark flashes. The usual time of onset is within twelve to twenty-four hours after injection, but we have seen several reactions which the patient did not bring to our attention until the second day. Our series of cases indicates distinctly that eye reactions, if they are to appear at all, appear within the time of the first five injections (91 per cent.), and that a patient who has had one course without eye trouble may be treated thereafter, so far as our experience goes (three courses), without trouble. In the opinion of observers with larger experience than ours, the dosage does not seem to be the invariable determining factor.

Following the warnings of Lorenz and Loevenhart, we accepted at first, as absolute contraindications to the use of tryparsamide, any ophthalmologic evidence that there had been previous syphilitic involvement of the optic nerve or indeed of the choroid or retina. We presently found that old choroiditis was not a contraindication, and within the last few weeks have placed two patients with optic atrophy on treatment with tryparsamide without any evidence of advance of the process. One patient, whose optic atrophy we believe we had hastened, was found, on further study of the history, to have shown evidence of a similar rate of progress before tryparsamide was begun.

CASE 5.—*A Man, Aged 42, Typical Paralytic With Definite Clinical but Little Serologic Response. Note the Fall in Cell Count and Diminished Intensity of First Zone Colloidal-Benzoin Test*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid				Clinical Status
					Wassermann Test	Nonne	Cells	Colloidal-benzoin	
Infection 1908 to 10/31/22	Elsewhere, arsphenamin	37 (?)	14.5 gm.	+++	+++ with 0.4, 0.6 and 1 c.c.	Positive	35	333330133331000	Strongly suggests dementia paralytica; confused and apathetic
	Mercury intramuscularly	18 (?)							
	Mercuric inunctions	300 (?)							
11/ 7/22 to 12/22/22	Arsphenamin	9	3.9 gm.	.....	.....	.....	..	.....	Marked hyperirritability after first course of treatment
	Swift-Ellis-Ogilvie, intraspinal	3	75 c.c. serum						
	Mercuric succinimid	10	1.33 grains (0.08 gm.)						
	Sodium iodid, intravenously	12	112.5 gm.						
12/18/22	.....	...	.....	+++	+++ with 0.4, 0.6 and 1 c.c.	Positive	11	333330333300000	
1/ 3/23 to 3/ 7/23	Tryparsamide	10	17 gm.	.....	.....	.....	..	.....	Working every day now; a little less irritable
3/23/23	.....	...	.....	(K) 44	(K) 44444	Positive	4	013300000000000	
6/ 5/23 to 8/21/23	Tryparsamide	10	29 gm.	(K) 44	(K) 44444	Positive	5	333202333300000	Little change, although working steadily; less irritable
	Mercuric salicylate	5							
12/13/23 to 2/14/24	Tryparsamide	8	24 gm.	(K) 44	(K) 44444	Positive	3	023100033100000	Remission? Working steadily; markedly less irritable; feels better, sleeps well; memory improved
	Mercuric salicylate	7	7 grains (0.46 gm.)						

CASE 6.—*A Man, Aged 36, Tabetic, With Severe and Persistent Gastric Crises, Under Observation and Treatment for Seven Years, Was Relieved and Returned to Work After Tryparsamide Treatment After all Other Measures had Failed*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid				Clinical Status
					Wassermann Test	Nonne	Cells	Colloidal-benzoin	
Infection 1902									
9/29/17 to 10/31/17	Arsphenamin.....	6	2.6 gm.	++++	++++	Positive	R. B. C.	.....	Gastric crises; pains and girdle sensations have disappeared
	Mercuric succinimid	21	3.5 grains (0.22 gm.)						
10/31/17 to 7/ 8/20	Neo-arsphenamin...	8	4.8 gm.	Negative	+++ with 0.3, 0.4 c.c.	Positive	152	0005542000	Crises; morning nausea; quit work
	Mercuric salicylate..	4	4 grains (0.26 gm.)						
	Mercuric inunctions	120	240 gm.						
7/ 9/20 to 9/24/20	Arsphenamin.....	5	1.3 gm.	Negative	Negative with 0.3, 0.4 and 1 c.c. (negative with 0.4, +++ with 1 c.c. chol. ant.)	Negative	3	.....	Still has crises
	Mercuric succinimid	15	2.5 grains (0.16 gm.)						
	Swift-Ellis-Ogilvie, intraspinal	6	150 c.c. serum						
9/25/20 to 1/10/21	Mercuric inunctions	30	60 gm.	Negative	Negative with 0.4 and 1 c.c. also chol. ant.	Negative	3	.....	Five crises; last 12 to 18 hours; not working
1/11/21 to 2/23/21	Arsphenamin.....	3	0.7 gm.	Negative	Negative with 0.4 and 1 c.c.	Positive	5	.....	Crises with each treatment
	Swift-Ellis-Ogilvie, intraspinal	4	100 c.c. serum						
2/24/21 to 7/15/21	Mercuric inunctions	40	80 gm.	Negative	Negative with 0.4 and 1 c.c. also chol. ant.	Negative	5	.....	Had four gastric hemorrhages; not working
7/16/21 to 8/24/21	Mercuric succinimid intramuscularly	20	5 grains (0.3 gm.)	.....	.....	.....	..	.....	Appetite improved; sleeping better
	Sodium iodid, intravenously	19	282.5 gm.						
8/25/21 to 11/ 1/21	No treatment.....	...	.....	.....	.....	.....	..	.....	Mild crises every week; no pain; not working
11/ 1/21 to 12/14/21	Mercuric succinimid, intramuscularly	27	6.75 grains (0.44 gm.)	.....	.....	.....	..	.....	Two crises during course
	Sodium iodid, intravenously	22	297.5 gm.						
12/15/21 to 5/16/22	Mercuric inunctions	40	80 gm.	Negative	Negative with 0.4, 0.6 and 1 c.c.	Negative	3	.....	Crises of ten days; not working
5/16/22 to 7/16/23	Mercuric inunctions	40	80 gm.	Negative	(K) negative	Negative	2	0000000220000000	Nausea every week or ten days; not working
7/17/23 to 9/24/23	Tryparsamide.....	10	27 gm.	.....	.....	.....	..	.....	No nausea; no crisis; resumed work
	Mercuric salicylate..	10	10 grains (0.65 gm.)						
9/24/23 to 2/12/24	No treatment.....	...	.....	Negative	.....	.....	..	.....	No nausea; no crisis; working
2/13/24 to 4/ 7/24	Tryparsamide.....	8	15 gm.	Negative	.....	.....	..	.....	No nausea; no crisis; working
	Mercuric salicylate..	8	8 grains (0.52 gm.)						

CASE 7.—*A Man, Aged 28, Had Typical Paresis With Phenomenal Symptomatic, but Much Less Serologic Response*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid				Clinical Status
					Wassermann Test	Nonne	Cells	Colloidal-benzoin	
Infection 1916									
1916 to 6/15/21	Elsewhere, arsphenamin, intravenously	19	7.6 gm.	+++	+++ with 0.4 and 1 c.c.	Positive	32 large leukocytes 160 small leukocytes	.....	Headaches only complaint
	Mercuric chlorid intravenously	14	9 grains (0.6 gm.)						
	Mercuric salicylate, intramuscularly	16	16 grains (1.04 gm.)						
6/16/21 to 8/18/21	Arsphenamin.....	7	2.2 gm.	Negative	+++ with 0.4 and 1 c.c.	Negative	13	3543444333	Feels about the same
	Mercuric succinimid	27	6.75 grains (0.44 gm.)						
	Swift-Ellis-Ogilvie, intraspinal	4	100 c.c. serum						
8/19/21 to 10/19/21	Mercuric inunctions	28	54 gm.	Negative	+++ with 0.4 and 1 c.c.	Negative	29	5554320000	Has jaundice
10/20/21 to 1/12/22	Arsphenamin, intravenously	8	3.1 gm.	Negative	+ with 0.4 c.c., ++ with 0.6 and 1 c.c.	Negative	5	5555512110	Still has headache
	Swift-Ellis-Ogilvie, intraspinal	6	150 c.c. serum						
	Mercuric succinimid, intramuscularly	29	7.2 grains (0.59 gm.)						
	Sodium iodid, intravenously	28	407.5 gm.						
1/13/22 to 5/16/22	No treatment.....	...	.....	+++	+++ with 0.4, 0.6 and 1 c.c.	Positive	17	.....	Headache
5/17/22 to 7/ 1/22	Arsphenamin.....	14	8.1 gm.	++	+++ with 0.4, 0.6 and 1 c.c.	Positive	6	3300000100000000	Says mind is sluggish
	Swift-Ellis-Ogilvie, intraspinal	4	100 c.c. serum						
	Mercuric succinimid	20	5 grains (0.32 gm.)						
	Sodium iodid, intravenously	18	175 gm.						
7/ 1/22 to 11/14/23	No treatment.....	...	.....	.....	(K) 4442 –	Positive	15	3333302333000000	Marries; committed to asylum; megalomania; maniacal
11/15/23 to 1/18/24	Tryparsamide.....	10	28 gm.	.....	(K) 41 – – –	Positive	3	0233003333000000	Quieter, still has ideas of grandeur
	Mercuric salicylate..	9	9 grains (0.6 gm.)						
1/19/24 to 3/ 8/24	No treatment.....	...	.....	(K) negative	(K) 44 – – –	Positive	4	0333302333320000	Calm and collected; facies good; biting lip and ptyalism
3/ 9/24 to 5/13/24	Tryparsamide.....	10	28 gm.	(K) negative	(K) 44 – – –	Positive	3	1333331233200000	Phenomenal response; mind clear; memory better; insight returns
	Mercuric chlorid.....	6	7 grains (0.46 gm.)						

PRECAUTIONS TO BE TAKEN IN CONTROLLING EYE COMPLICATIONS

Our mistake at the outset in controlling the eye complications of our patients consisted in an overemphasis on the history of such complications previous to treatment, and on the results of ophthalmoscopic examination of the fundus. We employed only tests for central vision, and rough tests of the visual fields. As a result, the first and only serious organic damage to a patient's eyes came on insidiously in the form of a concentric contraction of the visual fields, without central scotoma. Repeated examinations of the fundus of this patient were negative, and since his central vision was good he was reported as having normal visual acuity until his fields had narrowed to the point of tubular vision and he could no longer get about without stumbling because he could not see his feet. After this experience we realized that the accurate plotting of visual fields with the perimeter, and the determination of visual acuity before treatment is begun, with their frequent rechecking, especially during the first course, is absolutely essential to a proper control of the eye factor in tryparsamide treatment.

In our earlier experience with the drug, we discontinued treatment at once on the slightest complaint of any eye symptom from the patient. This excess of caution, we believe, contributed to a low percentage of organic damage. On the other hand, we later learned that subjective symptoms, if unaccompanied by signs of organic damage such as reduced vision and contracted fields, could be disregarded to some extent in urgent cases, and that no ill-effect followed the continuance of treatment once the symptoms had subsided. Again, emphasis must be placed on the examination of the vision and fields as the final test of damage. But under no circumstances should treatment be continued in the presence of a subjective complaint without an immediate objective examination. Ophthalmoscopic examination and tests of vision without perimentric fields, it must be reiterated, cannot be regarded as safe guides to visual damage.

Lillie's summary of our joint experience with the patients in this series points out that central scotoma does not necessarily occur in patients who nonetheless sustain marked damage to vision. He emphasizes the fact that not all damage to the eye detected in the course of tryparsamide treatment is due to tryparsamide. At least an equal amount is the result of syphilis, either active in the past, or progressing during treatment and in spite of it. The careful and complete examination of the eyes prior to treatment is, therefore, necessary as protection to both physician and patient. Lillie [14] further believes from the evidence

14. Lillie, W. I.: "Tryparsasmide in Syphilis of the Central Nervous System." Observations from the Ophthalmologic Standpoint, J. A. M. A. **83**:809 (Sept. 13), 1924.

in this series that arsphenamin in patients with neurosyphilis may give rise to damage to vision not unlike that produced by tryparsamide, which may be wrongly ascribed to tryparsamide instead of to previous arsphenamin treatment, unless preliminary examination is carefully carried out.

In general, there seems to be no question that the risk to the eyes in the treatment with tryparsamide is real, and under faulty, careless, inexperienced, or inexpert management, the risk may be very great. Our four patients who had only subjective symptoms recovered completely. Of the eight who had objective evidence of damage in the form of contraction of fields, only three were reexamined after an interval of several months after treatment, and all had recovered, one having even larger fields and better vision than he had before treatment. We believe that if systematic examination of vision and the taking of perimetric fields is carried out before treatment and at frequent intervals during treatment, if every eye complaint is made the signal for such an examination and treatment is at once discontinued when any signs of organic damage appear, if the patient is warned what to be on the look-out for and taught to cooperate but not encouraged to become over-concerned, and moderate dosage such as is now in use is not exceeded, the eye complications following treatment with tryparsamide will be reduced to a minimum, and recovery from such complications as develop will be the rule. Whether the risk of partial or complete blindness will be small enough to give such treatment precedence over the risks of standard treatment, including that of sulpharsphenamin dermatitis, and of myelitic reactions from intraspinal treatment, remains to be seen. In any event, we do not feel that the situation is as yet sufficiently clear, even to those who have had more experience with the drug, to make it advisable to place tryparsamide on the market for general use. We are still disposed to regard tryparsamide as a last, rather than a first, resort in the treatment of asymptomatic neurosyphilis, and to advise that patients with this complication of the disease be intensively treated by standard methods before the new drug is employed. In cases of early paresis with confirmatory symptoms and signs, tryparsamide may be considered at the outset, provided the patient and the responsible relatives are fully informed as to the purpose, the probable benefits and the risks involved. In late paresis with definite deterioration, we have seen no evidence that tryparsamide has distinctive advantages, either clinically or serologically, which justify its extensive employment. The ideal field for its action is in resistant asymptomatic neurosyphilis which withstands intensive standard treatment and early paresis before deterioration sets in. The combination of tryparsamide with other antisyphilitic medication, and the effect of prolonged use of the drug in the production of ultimate cure or arrest of the disease are as yet untouched by our experience.

CASE 8.—*A Man, Aged 41, With Asymptomatic Paralysis, Becoming Violent and Requiring Institutional Care While Under Standard Treatment, Steadily Improved Under Tryparsamide, and Became Mentally Normal. This Patient Had a Toxic Dermatitis from Arsphenamin, but Took Tryparsamide Without Cutaneous Reaction*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid				Clinical Status
					Wassermann Test	Nonne	Cells	Colloidal-benzoin	
Infection 1898 to 6/18/18	Arsphenamin.....	2	0.8 gm.	Negative	Negative with 0.2, 0.3, 0.4 and 0.5 c.c.	Negative	73	.....	Nervous; stomach trouble
6/ 8/18 to 3/ 8/19	Arsphenamin.....	1	0.3 gm.	Negative	+++ with 0.3 and 0.4 c.c.	Positive	92	0001221000	The same
3/ 8/19 to 4/15/19	Arsphenamin.....	6	2.2 gm.	Negative	Negative with 0.3 c.c., + with 0.4 c.c.	Negative	18	.....	Not so nervous; stomach better
	Mercuric succinimid	20	3 grains (0.19 gm.)						
	Spinal drainage.....	3	120 c.c.						
4/16/19 to 11/24/19	Mercuric inunctions	40	80 gm.	Negative	+++ with 0.3 and 0.4 c.c.	Positive	103	5555443210	Stomach better; difficulty in starting urination
11/24/19 to 2/ 6/20	Arsphenamin.....	11	4.0 gm.	.....	+++ with 0.3 and 0.4 c.c.	Negative	3	3443321100	Has toxic dermatitis; looks nervous and shaken
	Neo-arsphenamin...	1	0.4 gm.						
	Sodium iodid, intravenously	14	142 gm.						
2/ 7/20 to 4/ 7/20	No treatment.....	...	.....	.....	+ with 0.3, +++ with 0.4 c.c.	Positive	5	5554322100	Feels somewhat better
4/ 8/20 to 6/ 8/20	Neo-arsphenamin...	4	0.8 gm.	Negative	Negative with 0.3 and 0.4 c.c.	Positive	5	.....	More toxic dermatitis; had to resort to foreign serum
	Swift-Ellis-Ogilvie, intraspinal, donor's serum	5	125 c.c. serum						
6/ 9/20 to 8/21/20	Mercuric inunctions	15	30 gm.	.....	Negative with 0.3 and 0.4 c.c.	Negative	5	.....	Gained 15 pounds (6.9 kg.); looks fine; mild shooting pains
8/22/20 to 10/19/20	Swift-Ellis-Ogilvie, intraspinal, donor's	5	135 c.c. serum	Negative	+ with 0.4 c.c., +++ with 1 c.c.	Positive	5	0112100000	Again has toxic dermatitis
	Mercuric salicylate	9	9 grains (0.6 gm.)						
	Sodium iodid, intravenously	2	15 gm.						

10/20/20 to 2/ 1/21	Mercuric salicylate	3	3 grains (0.19 gm.)	Negative	Negative with 0.4 and 1 c.c.	Negative	1	.....	Palpitation
2/ 1/21 to 3/ 4/21	Swift–Ellis–Ogilvie, intraspinal, donor's	3	75 c.c. serum	.....	Negative with 0.4 and 1 c.c.	Negative	2	.....	Striking result
3/ 5/21 to 8/15/21	Mercuric salicylate	5	5 grains (0.26 gm.)	Negative	+ + with 0.4, + + + with 1 c.c.	Positive	61	0001211100	Looks fine; complete relapse
	Mercuric inunctions	25	50 gm.						
8/16/21 to 11/17/21	Swift–Ellis–Ogilvie, intraspinal, donor's	6	150 c.c. serum	.....	+ + with 0.4, + + + with 1 c.c.	Positive	14	55444300000	Overtreatment syndrome; nervous and fidgety; toxic dermatitis; on vacation
	Mercuric succinimid	36	9 grains (0.6 gm.)						
	Sodium iodid, intravenously	30	512.5 gm.						
11/18/21 to 7/20/22	No treatment.....	...	.....	Negative	+ + + with 0.4, 0.6 and 1 c.c.	Positive	6	55555431	Still has stomach trouble
7/21/22 to 8/ 9/22	Arsphenamin.....	1	0.2 gm.	.....	.....	.....	..	.....	Marked toxic dermatitis
	Mercuric succinimid	4	1 gm.						
8/ 9/22 to 10/ 4/22	No treatment.....	...	.....	.....	+ + + with 0.4, 0.6 and 1 c.c.	Positive	17	3333300033700000	Looks worried; nervous; stomach trouble; working hard
10/ 5/22 to 11/ 8/22	Neo-arsphenamin...	3	1.0 gm.	.....	+ + + with 0.4, 0.6 and 1 c.c.	Positive	24	3333303333000000	The same
	Swift–Ellis–Ogilvie, intraspinal	3	75 c.c. serum						
11/ 8/22 to 7/ 9/23	No treatment.....	...	.....	.....	(K) 4444 –	Positive	4 l. l., 14 s. l.	3333333333331000	Better, but quite nervous; slow to comprehend
7/10/23 to 9/11/23	Tryparsamide.....	10	26 gm.	.....	(K) 4444 –	Positive	10	0123103333300000	Feels better than in years; less depressed; going back to practice
	Mercuric salicylate..	10	10 grains (0.65 gm.)						
9/11/23 to 11/17/23	No treatment.....	...	.....	(K) 1 –	(K) 444 – –	Positive	2	0233000332000000	Actively engaged in practice; memory excellent; weight normal
11/17/23 to 1/19/24	Tryparsamide.....	10	28 gm.	.....	(K) 444 – –	Positive	1	0122002333200000	Working hard; looks fine
	Mercuric salicylate..	9	9 grains (0.6 gm.)						
1/19/24 to 3/22/24	No treatment.....	...	.....	.....	(K) 441 – –	Positive	5	0022003333200000	Feels and looks well; working steadily
3/23/24 to 5/26/24	Tryparsamide.....	10	21 gm.	(K) 42	(K) 44 – – –	Positive	3	0000002320000000	Feels fine; actively engaged in practice

CASE 9.—*A Man, Aged 41, With Well Defined Paralysis, Under Observation and Treatment for Six Years, Illustrating the Failure of Every Form of Modern Treatment, Showed Remarkable Symptomatic and Progressive Serologic Improvement under Tryparsamide*

Dates	Drugs	Doses	Dosage	Blood Wassermann Reaction	Cerebrospinal Fluid				Clinical Status
					Wassermann Test	Nonne	Cells	Colloidal-benzoin	
Infection 1898 to 8/13/18	Elsewhere, mercuric salicylate	8	8 grains (0.52 gm.)	+++	+++ with 0.3 and 0.4 c.c.	Positive	285	0454320000	Nervous and fidgety; slurring speech; tremor of extended hands
8/15/18 to 9/18/18	Arsphenamin.....	6	2.6 gm.	Negative	+++ with 0.3 and 0.4 c.c.	Positive	73	0445555422	Extraordinary well-being; weak, and walk is unsteady
	Mercuric succinimid	21	3.5 grains (0.22 gm.)						
	Spinal drainage.....	5	169 c.c.						
9/18/18 to 1/22/19	Mercuric inunctions	40	80 gm.	Negative	+++ with 0.3 and 0.4 c.c.	Positive	71	0112211000	Euphoric; worked during absence
1/22/19 to 3/ 4/19	Arsphenamin.....	11	4.8 gm.	Negative	+ with 0.3 and 0.4 c.c.	Positive	16	0012211000	In fine shape
	Mercuric succinimid	11	2 grains (0.13 gm.)						
	Sodium iodid, intravenously	9	83 gm.						
	Spinal drainage.....	3	136 c.c.						
3/ 5/19 to 4/16/19	Mercuric inunctions	24	48 gm.	Negative	Negative with 0.3 and 0.4 c.c.	Positive	10	0000000000	Looks good; aches all over
4/17/19 to 7/ 5/19	Arsphenamin.	7	2.7 gm.	Negative	Negative with 0.3 and 0.4 c.c.	Positive	4	.....	Had jaundice; feels well
	Swift-Ellis-Ogilvie, intravenously	2	50 c.c. serum						
	Sodium iodid, intravenously	3	18 gm.						
7/ 6/19 to 4/19/21	Arsphenamin.....	1	0.5 gm.	.....	+++ with 0.4 and 1 c.c.	Positive	5 poly, 113 s. l.	0430000000	Speech slurring and hesitating; facies mask-like; memory poor; fussy; very irritable
4/20/21 to 6/ 6/21	Arsphenamin.....	12	6 gm.	.....	+++ with 0.4 and 1 c.c.	Positive	2	4555331000	Talks, acts and looks better
	Mercuric succinimid	18	4.5 grains (0.29 gm.)						
	Swift-Ellis-Ogilvie, intraspinal	3	75 c.c. serum						

6/ 7/21 to 16/17/21	Mercuric inunctions	40	120 gm.	++	Negative with 0.4 c.c., +++ with 1 c.c.	Positive	4 l. l. 84 s. l.	5553220000	Calmer; not so flighty
10/18/21 to 12/27/21	Arsphenamin..... Mercuric succinimid Swift-Ellis-Ogilvie, intraspinal Sodium iodid, intravenously	5 35 5 25	2 gm. 9 grains (0.6 gm.) 125 c.c. serum 467.5 gm.	.....	+ with 0.4, negative with 1 c.c.	Negative	1	5555554200	In remission? Still speech defect; paretic mannerisms
12/18/21 to 8/14/22	No treatment.....	...	.....	+++	+++ with 0.4, 0.6 and 1 c.c.	Positive	6 l. l. 57 s. l.	0033003332000000	Looks surprisingly well; facies more alert; speech crisp and clear cut
8/15/22 to 9/15/22	Arsphenamin..... Swift-Ellis-Ogilvie, intraspinal	5 5	1.6 gm. 125 c.c. serum	.....	+++ with 0.4, 0.6 and 1 c.c.	Positive	7	.....	Emotional instability; feels better than in years
9/15/22 to 1/29/23	No treatment.....	...	.....	(K) 44	(K) 4444 -	Positive	60	.....	Quite emotional
1/30/23 to 4/ 4/23	Tryparsamide..... Mercuric succinimid Mercuric salicylate	10 19 6	30.5 gm. 3 grains (0.19 gm.) 6 grains (0.4 gm.)	(K) 44	(K) 4441 -	Positive	4	0000000033000000	Marked general improvement; speech, no tremor or slurring
4/ 4/23 to 6/ 4/23	No treatment.....	...	.....	(K) 44	(K) 443 - -	Positive	6	0000003332000000	Wife says he is better than in five years; helped more in business; speech fairly distinct; sleeps well
6/ 5/23 to 8/ 8/23	Tryparsamide..... Mercuric salicylate..	10 10	30 gm. 10 grains (0.65 gm.)	(K) 44	(K) 44 - - -	Positive	7	0000003320000000	A little upset; nervous
8/ 9/23 to 10/ 9/23	No treatment.....	...	.....	(K) 42	(K) 44 - - -	Negative	3	0000002332000000	Looks fine; speech clear; facies sharper cut; more responsibility at home
10/10/23 to 12/12/23	Tryparsamide..... Mercuric salicylate..	10 7	30 gm. 7 grains (0.46 gm.)	(K) 44	(K) 431 - -	Negative	1	0000000323200000	A different man; facies sharpening
12/13/23 to 5/27/24	No treatment.....	...	.....	(K) 4 -	(K) 41 - - -	Positive	1	0000003320000000	A changed man; hard to recognize the paretic element

CONCLUSIONS

1. While results of by no means negligible value can be secured in the treatment of neurosyphilis by standard methods, tryparsamide is, in our experience, superior both clinically and serologically for the treatment of the resistant case of neurosyphilis.

2. So far as our eighteen months of experience goes, we find the clinical effects much more striking than the serologic, but the latter are undoubtedly present and may be improved on with time and the development of new and better treatment combinations.

3. The most striking serologic responses in the spinal fluid are in the cell count, globulin content and colloidal tests.

4. The delicacy of the Wassermann test used is a factor in comparative results.

5. Tryparsamide treatment is superior to other forms of treatment for neurosyphilis on the score of minimal expense, inconvenience and loss of time, and maximal symptomatic gain in mental cases.

6. Eye complications constitute, however, a definite risk, of which patient and physician should be fully aware.

7. An examination of the eyes by a competent ophthalmologist, with special reference to visual acuity and perimetric fields, must precede the first administration of the drug, and be repeated several times, especially during the first injections of the first course, when complications seem most likely to arise.

8. Subjective symptoms, such as dimming of vision, blurring, sensation as of bright clouds in the peripheral field, flashes of light, sense of grayness and difficulty in seeing the feet in stepping up, are all important and should be the signals for immediate testing for objective damage.

9. It may be possible, in case of necessity, to continue treatment in the face of subjective symptoms if no objective evidence of injury is found. But if even slight objective impairment has occurred, we advise for the time being, the absolute discontinuance of tryparsamide treatment.

10. Tryparsamide produces a definite Herxheimer-like flare-up of symptoms in mental cases, which must be allowed for in making plans for treatment, and may necessitate temporary custodial care of the patient with special nursing, restraint, and precautions against violence and self-injury.

11. The social values in a given case should be considered with reference to increased sexual activity in certain patients, and with reference to the possibility of the conversion of an unobjectionable and harmless patient into an objectionable and dangerous one.

12. Tryparsamide appears to have a beneficial effect on patients with resistant tabes, including gastric crises, even though the spinal fluid may be negative.

13. Our results in the treatment of late paresis by tryparsamide in an institution for the insane are disappointing and do not lead us to continue it in this field. The unfavorable progress of certain unfavorable cases may apparently be hastened by the drug.

14. We are still disposed to regard tryparsamide, because of the possibility of eye complications, as a last rather than a first therapeutic resort in asymptomatic neurosyphilis. In obvious early paresis, we recommend its use after or in conjunction with other forms of treatment. The experience of other observers has established its unfitness for use in most other aspects of syphilis, owing to its lack of spirillicidal power.

DISCUSSION

Dr. Udo J. Wile, Ann Arbor, Mich.: I have had some experience with tryparsamide, just one-third that of Dr. Stokes. I reported the results in fifty cases, a preliminary report, at the annual meeting of the American Medical Association. I have submitted a draft of my paper to Dr. Brown, and he has reported to me that our findings are in accord with what he would like to have said in view of our experience.

Because many of these cases were drawn from the psychopathic department rather than from my own practice, most of the patients have been paralytic. My results have been quite different from the results of those who have preceded me, and probably are different from the results of those who will follow me. I think this is to be expected, because we all employ different methods in laboratory technic and in the interpretation of results, and the personal element must be considered, especially regarding improvement. For instance, I see a great difference in Dr. Stokes' interpretation and mine regarding the Wassermann reaction. I have interpreted no improvement where he would interpret improvement according to different criteria. My cases have shown reactions from ++++ to ++, but I would not call such change improvement. Dr. Stokes would, because he believes this indicates improvement. I have never been able to convince myself that there is much difference between a ++++ reaction and a ++ reaction. Which is the right view, will remain to be shown in the future.

The change for the better in our cases has been one of well-being, of apparent orientation from disorientation, and the findings have not been parallel in my experience, brief as it is, with coincident changes in the fluid. My experience is unlike his, for I have not been able to affect the pain in tabes and he has.

I feel most hopeful regarding the effect of tryparsamide in the diffuse cerebrospinal cases. Here, to be sure, we already have admirable means of combating the infection, and we should try the tryparsamide in those cases only as a promising method added to the means we already have at our disposal.

As to the untoward results, in 345 injections, because of the great care exercised in choice of patients, we have not seen any untoward results. One

patient vomited for an hour or so after the injection, but there was no other reaction.

I wish to emphasize the necessity of careful ophthalmoscopic examination, as Dr. Stokes has pointed out.

Dr. Jay Frank Schamberg, Philadelphia: I have had no practical experience with tryparsamide, but I think without that a reference to some of the differences between tryparsamide and some of the arsphenamins might not be without profit. It has long been known that arsphenamin is a colloidal substance. It cannot be produced chemically pure. It is impossible to purify it by repeated crystallization. Ehrlich felt that the conversion of pentavalent arsenic to the trivalent form was a great step forward. The trivalent form is more destructive to the spirochete than pentavalent arsenic. But the arsphenamins, which are trivalent by reason of their colloidal nature, may not be able to penetrate the choroid plexus and reach the nerve cells in sufficient concentration.

This new tryparsamide has certain advantages. It is a crystalloid substance and is more readily diffusible and gets into the nervous system more readily and by reaching the nervous tissue in larger quantity than does arsphenamin may conceivably produce a better effect. Because it is a crystalloid it may be purified by repeated crystallization and made free of the impurities found in arsphenamin. It is, therefore, freer of reactions. We know that atoxyl has a particular affinity for the nervous system, as was observed in the treatment of sleeping sickness; tryparsamide is a derivation of atoxyl. We have here a product which has primarily a greater affinity for nerve structure and one which probably reaches it in greater concentration. This may explain some of the differences between the therapeutic results obtained with tryparasamide and the other arsenicals.

Dr. John H. Stokes, Philadelphia: The charts which accompany the published account of this work will, I think, help to bear out our estimate of the value of the quantitative Wassermann test in judging of the gradual serologic improvement of the patients. The other points are covered in sufficient detail in the complete publication. Much emphasis should be laid on the fact that this drug is not intended for or adapted to the ordinary treatment of syphilis, and especially of early syphilis. I personally do not feel that it should be used alone in first instance, even in the treatment of early neurosyphilis, which should be treated as syphilis quite as much as neurosyphilis. I feel that tryparsamide, because of the eye complications, should still rank as a last and not a first resort, except in obvious early paralysis. There seems to me to be reason to believe, as I think Moore has also noted, that preliminary treatment for syphilis by standard methods improves the response to tryparsamide. The best methods of using the drug cannot be regarded as fully determined as yet. That it is a most welcome aid in resistant neurosyphilis, is an opinion fully justified by our experience.

URTICARIA PIGMENTOSA WITH HYPERPLASIA OF THE THYMUS GLAND*

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Two consecutive cases of urticaria pigmentosa in which an enlarged thymus gland was easily demonstrated by roentgen-ray examination came under my observation.

Three years ago I was asked by Dr. William Harvey Guy to study a case of nodular type of urticaria pigmentosa from an endocrinologic standpoint, and much to our mutual surprise we found a marked hyperplasia of the thymus gland in association with a slight adenopathy of the cervical glands. I was tempted to report this observation at that time. However, it was thought wise to wait and see what other cases might show.

On Sept. 10, 1924, a macular type of urticaria pigmentosa came under my observation with similar findings, and I feel that even though the co-appearance of these two relatively rare conditions may be coincidental, the observation is useful and worthy of record.

The comparative infrequency with which the dermatologist is faced with the thymus gland necessitates a brief description of the known anatomic, physiologic and pathologic facts regarding this organ, in order to show certain other correlative factors in these two pathologic entities: urticaria pigmentosa and hyperplasia of the thymus gland.

ANATOMY OF THE THYMUS GLAND

The thymus gland [1] arises in man as a paired ventral outgrowth from the entoderm of the third and fourth branchial clefts. Its original form is that of a flat pouch. With gradual thickening of the walls of the sac, the original lumen is obliterated. It is composed of two lobes, which is turn are formed from a great many lobules.

Two types of cells are distinguishable in the thymus—one resembling the lymphocyte forming the cortex of the organ, the other, epithelial in nature, occurring throughout, but less marked in the central part.

The gland [2] at birth lies behind the sternum between the pericardium and great vessels of the upper extremity, extending upward into the region of the neck.

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* From the dermatological department of the Pittsburgh Skin and Cancer Foundation.

1. MacCallum, W. G.: A Text Book on Pathology, Ed. 3, Philadelphia, W. B. Saunders Company, 1821, p. 887.

2. Janeway, Henry H.: Lecture Notes on Physiology, The Ductless Glands, New York, Paul B. Hoeber, 1817, p. 52.

EVOLUTION AND INVOLUTION OF THE THYMUS GLAND

Unlike other organs, the thymus gland undergoes retrogressive changes. There seems to be a variance among the different authorities as to the time of this occurrence.

MacCallum[3] states that the thymus reaches its maximum development coincidentally with the maturation of the sexual organs, and then gradually atrophies. He quotes Hammar's tables of normal weights of the thymus gland at various ages as follows: new-born, 13.26 gm.; from 6 to 10 years, 26.1 gm.; from 11 to 15 years, 37.52 gm.; from 21 to 25 years, 24.73 gm.; from 56 to 65 years, 16.08 gm., and from 66 to 75 years, 6 gm.

Janeway [2] says that involution of the gland begins at the end of the second year, and the process is completed (by gradual replacement of the lymphoid tissue by fatty tissue) at adolescence.

Holt [4] says:

> Since the large thymus is so important an organ it is desirable to know what may be regarded as normal. Bovaird and Nicoll, who weighed the thymus in 495 consecutive autopsies in children under five years, found that the weight was greatest at birth, being 7.7 grams. After this time the change in weight was very slight for a period of five years, the average for the entire 495 observations being 5.9 grams, which was about the same as the average for each of the years taken separately. The average weight at birth was 6.5 grams; during infancy and childhood, 4 grams. The result of these observations do not differ essentially from those of Friedleben. It may therefore be assumed that the average weight of the normal thymus at birth is from 6 to 7 grams; from birth to five years from 3 to 4 grams. Anything over 10 grams may be considered distinctly abnormal.

Tidy [5] gives the weight of the gland at birth as 7 gm.; maximum at 2 years, about 10 gm. Atrophy then commences and after puberty is more rapid.

THE FUNCTION OF THE THYMUS GLAND

Berman [6] says that the thymus is the gland which dominates childhood. It appears to do so by inhibiting the activity of the testes and ovaries. Castration causes a persistent growth and retarded atrophy of the thymus. Removal of the thymus hastens development of the gonads.

There is evidence that the thymus is involved in the health and efficiency of muscle cells and muscularity.[7]

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3. MacCallum, W. G.: A Text Book on Pathology, p. 888.
4. Holt, L. Emmett: The Diseases of Infancy and Childhood, Ed. 5, New York, D. Appleton & Company, 1910, p. 879.
5. Tidy, Henry L.: A Synopsis of Medicine, New York, William Wood & Company, 1920, p. 709.
6. Berman, Louis: The Gland Regulating Personality, New York, The MacMillan Company, 1921, p. 85.
7. Berman, Louis: The Gland Regulating Personality, p. 87.

Janeway [8] thinks that the function of the thymus has to do with ossification and development of bones, while Park and McClure [9] obtained negative results after extirpation of the organ.

Tidy [5] says that the functions of the organ are unknown, and following extirpation results are variable and doubtful; there may be none: and claims include conditions resembling rickets, cachexia, hypertrophy of testes. Evidence of internal secretion is slight. He thinks it is possibly a lymphoid organ.

Brown [10] says that the rôle of this gland is normally limited to the infantile period. With the development of the gonads, its activity ceases.

In general, one is safe in assuming that no special function of the body has as yet been definitely attributed to the thymus gland. Although there seems to be an antagonism between it and the gonads, this is hard to explain, since there is as yet no evidence of an internal secretion formed by the thymus.

HYPERPLASIA OF THE THYMUS GLAND

This occurs in the following conditions: (1) status thymicolymphaticus, 100 per cent. of cases; (2) myasthenia gravis, 90 per cent. of cases; (3) exophthalmic goiter, occasionally; (4) Addison's disease, occasionally; (5) leukemia, occasionally, and (6) acute infections affecting lymphoid tissues, occasionally.

The only one of these conditions which is of interest to the present discussion is the first mentioned, status thymicolymphaticus.

Holt [11] says that the term status lymphaticus is applied to a definite pathologic condition, which is associated with clinical manifestations less constant and not characteristic. The most striking part of the lesion is the great enlargement of the thymus gland, with which is found a hyperplasia of lymphoid tissue throughout the body.

> In the status lymphaticus the thymus is often from five to ten times larger than normal. The lymph nodes of the tracheo-bronchial region are greatly enlarged. Those of the mesenteric region may be still larger. Peyer's patches are very prominent and the solitary follicles of the small intestine appear like mustard seeds upon the folds of the mucous membrane. Those of the colon are also very prominent. The lymphoid tissues about the pharynx and all the lymph nodes of the body are greatly hypertrophied. The spleen is usually enlarged, with prominent follicles.

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8. Janeway, Henry H.: Lecture Notes on Physiology, The Ductless Glands, p. 204.

9. Park, Edwards A., and McClure, Roy D.: The Results of Thymus Extirpation in the Dog with a Review of the Experimental Literature on Thymus Extirpation, Am. J. Dis. Child. **18**:317 (Nov.) 1919.

10. Brown, W. Langdon: International Medical Annual, New York, William Wood & Company, 1922, p. 137.

11. Holt, L. Emmett: The Diseases of Infancy and Childhood, p. 880.

Timme [12] says that status thymicolymphaticus is usually accompanied by inadequate suprarenals, and the external characteristics of one are similar to those of the other state. The patient is prone to suffer from the various disturbances of a dystonic vascular or smooth muscle system, such as urticaria and angioneurotic edema.

The treatment of enlarged thymus glands is in the domain of radium therapy. Heublein,[13] in a paper which was illustrated by a series of roentgenograms showing the thymic shadows before and after treatment, described the technic definitely.

> The author has treated in all forty-one cases, and considers that the condition, as revealed by x-ray examination, is much more common than is usually supposed. The technique is fully explained: 200 mgrms. of radium element are applied over four areas on the anterior chest wall, filtered through 0.3 mm. of silver, at half an inch distance from the skin, for one hour in each place. Emphasis is laid on the point that in these small infants radium has great advantages over x-ray, as its application is simple and does not frighten the child.

URTICARIA PIGMENTOSA

Urticaria pigmentosa [14] was first described by Nettleship in 1869, and its present name was given by Sangster in 1878. Since then a great deal has been written, and the disease is a well-known dermatologic entity.

Its most important characteristics, besides its appearance, which is so well known that its repetition would be boresome, are:

1. It is essentially a disease of infancy.[15]

2. The disease [16] usually begins in the first few months of life, and it may be congenital.

3. The disease [17] is singularly persistent and may remain for years.

4. The disease [18] usually tends to disappear as puberty is reached.

5. The lesions [19] as a rule are symmetrical and tend to follow cutaneous lines of cleavage.

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12. Timme, Walter: Lectures on Endocrinology, New York, Paul B. Hoeber, 1924, p. 58.
13. Heublein, A. C.: Am. J. Roentgenol. **7**:191 (April) 1920.
14. Ormsby, Oliver S.: A Practical Treatise on Disease of the Skin, Ed. 2, Philadelphia, Lea & Febiger, 1921, p. 150.
15. MacLeod, J. M. H.: Diseases of the Skin, p. 690.
16. Pusey, William Allen: The Principles and Practice of Dermatology, Ed. 4, New York, D. Appleton & Company, 1924, p. 223.
17. Macleod, J. M. H.: Diseases of the Skin, New York, Paul B. Hoeber, 1921, p. 690.
18. Sutton, Richard L.: Diseases of the Skin, Ed. 5, St. Louis, C. V. Mosby Company, 1923, p. 136.
19. Highman, Walter J.: Dermatology, New York, The Macmillan Company, 1921, p. 49.

6. There is a general enlargement of the glands in a number of cases. Glands are described as hard and shotty,[20] not proceeding, however, to suppuration.[21]

Without drawing any conclusions, the points of similarity of urticaria pigmentosa and hyperplasia of the thymus gland seem apparent in that:

1. They are diseases of infancy principally.
2. Involution is slow.
3. There is a tendency to spontaneous cure at puberty.
4. There is general glandular enlargement.
5. The symmetrical tendency and the following of the lines of cleavage in urticaria pigmentosa consistently point to a metabolic disturbance.

CASE REPORTS

CASE 1.—*History.—Urticaria Pigmentosa, Nodular Type.* (Dr. W. H. Guy's case).—W. J. D., a boy, aged 8 months, American, was seen on June 14, 1921. The patient was referred to me by Dr. Guy for endocrine study after he established the diagnosis of urticaria pigmentosa. The boy presented a scattered generalized eruption affecting all parts of the body. The lesions were discrete, elevated, rounded and oblong, nodular yellowish masses, surrounded by a pinkish areola, varying in size from 0.04 to 2 cm. On rubbing, the lesions exhibited a marked urticarial tendency. One of the lesions on the back was capped by a bulla. This eruption began on the abdomen, at the age of 4 months, and since then it has increased, coming in crops.

The child was of normal delivery, and breast fed. There was evidence of glandular enlargement in the neck, groin and under the axilla. Roentgen-ray examination showed an enlarged thymus.

Course and Treatment.—The thymic area was divided into four areas, and were treated alternately as follows: On June 18, 1921, 50 mg. of radium were given at one-half inch distance for four hours over the thymus; on July 2, 50 mg. of radium at one-half inch distance for four hours over the thymus. From September 15 to 20 no new lesions appeared, but no appreciable change could be noted in the lesions. On September 21, the skin showed slight radium reaction, the lesions gradually fading.

I have no further notation on the case as I am unable to locate the boy.

CASE 2.—*Urticaria Pigmentosa, Macular Type.*—A. P., a boy, aged 16 months, Polish, was seen on Sept. 10, 1924. The boy presented a generalized maculopapular eruption which covered most of the body. The lesions, both discrete and mostly confluent, were flat, oblong yellowish-brown pigmentary patches, some slightly elevated, but most level with the skin. By friction, factitious urticaria was produced easily. The lesions seemed to follow the cutaneous lines of cleavage, and suggested the striped markings of a tiger described by Highman. Glandular enlargement in the neck and groin were easily discerned.

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20. Ormsby, Oliver S.: A Practical Treatise on Disease of the Skin, p. 151.
21. Morris, Malcolm: Diseases of the Skin, Ed. 6, New York, William Wood & Company, 1917, p. 97.

Fig. 1 (Case 1).—Dr. Guy's patient; urticaria pigmentosa, one lesion showing vesiculation.

Fig. 2 (Case 1).—Front view.

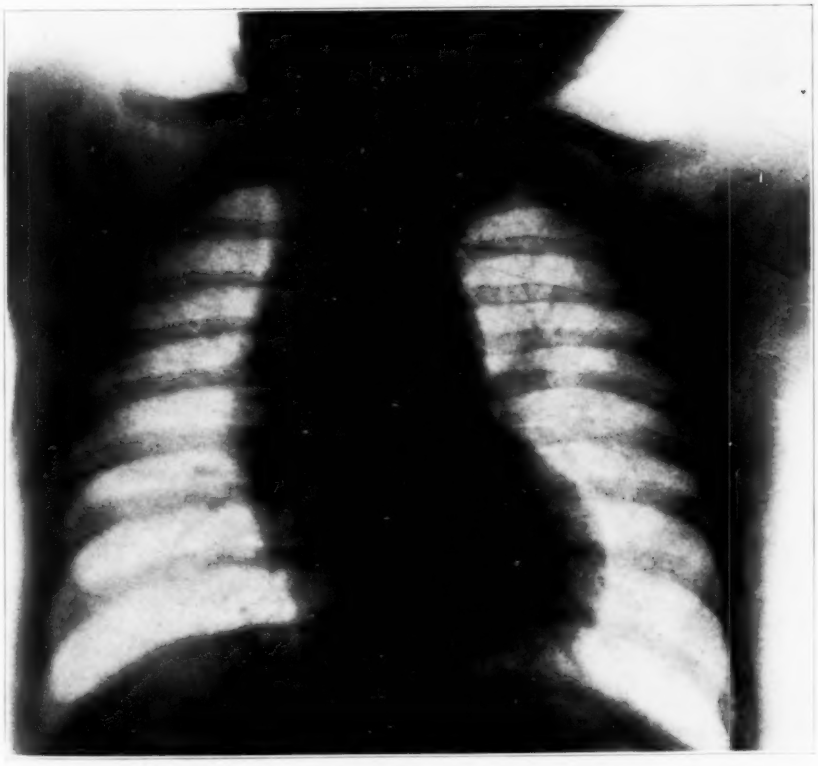

Fig. 3 (Case 1).—Hyperplasia of thymus.

Fig. 4 (Case 2).—Urticaria pigmentosa.

Fig. 5 (Case 2).—Urticaria pigmentosa.

Fig. 6 (Case 2).—Anterior view of hyperplasia of thymus.

Fig. 7 (Case 2).—Posterior view of hyperplasia of enlarged thymus.

The condition began at the age of 1 month and gradually spread over the entire surface.

The child was a full term baby, breast fed, one of four children, of whom one brother was living and well; two died at the age of 23 months and 2 months, respectively. The mother and father were living and well.

Roentgen-ray examination showed a markedly enlarged thymus gland.

SUMMARY AND CONCLUSIONS

1. The author reports two cases of urticaria pigmentosa showing hyperplasia of the thymus gland.

2. Some similarity between status thymicolymphaticus and urticaria pigmentosa is pointed out.

3. Treatment of the enlarged thymus with radium, followed by involution of urticaria pigmentosa, is described.

4. Further study for properly placing urticaria pigmentosa in the definite endocrine group of diseases is warranted.

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GLUCOSE TOLERANCE REACTIONS IN ECZEMA

A REPORT OF EIGHTY-SIX CONSECUTIVE CASES *

SAMUEL AYRES, JR., M.D.

LOS ANGELES

The first scientific work of any extent dealing with the carbohydrate metabolism in eczema and eczematoid eruptions was that reported recently by McGlasson.[1] McGlasson dealt only with the fasting blood sugar determinations. The following statistical study of the glucose tolerance reactions in eighty-six consecutive cases of typical eczema was undertaken in order to examine the carbohydrate metabolism in eczema in more detail.

The term "typical" eczema as used in this series applies to any one of the various phases through which an eczematous eruption may pass —erythema, edema, vesiculation, exudation, crusting, lichenification and desquamation. Aberrant types, such as papular eczema and infected eczema, are included, but eczematoid eruptions, such as epidermophytosis, frankly seborrheic dermatitis, dermatitis herpetiformis, erythema multiforme and conditions obviously due to local infections, are not included.

It is understood that this attempt at clinical differentiation runs the risk of being irrational, since much evidence points to an intimate relationship between eczema and some of the eczematoid eruptions. No attempt is made in this discussion to separate eczema from dermatitis. Dermatitis, in its broadest sense, means literally inflammation of the skin, which obviously should include erysipelas, furunculosis, etc. But eczema indicates a certain type of dermatitis, usually characterized at some stage of its development by the collection of fluid in the form of gross or microscopic vesicles, although the vesicular stage may be relatively brief. In other words, eczema is a symptom, a method of cutaneous reaction to various irritants, either internal or external, or a combination of the two.[2]

Aside from the above qualifications, no attempt was made to select the cases. Tests were made on both private and clinic patients whenever they could be persuaded to submit. Every effort was made to have the series represent the true state of the carbohydrate metabolism in clinical eczema, as the term is commonly understood.

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* From the Department of Dermatology, White Memorial Hospital.

1. McGlasson, I. L.: Hyperglycemia as an Etiologic Factor in Certain Dermatoses, Arch. Dermat. & Syph. **8**:665 (Nov.) 1923.

2. Darier, J.: A Text-Book of Dermatology, Philadelphia, Lea & Febiger, 1920, p. 60.

TABLE 1.—*Glucose Tolerance in Cases Studied by Author*

Case	Age	Sugar Excess in Diet	Distribution	Type	Glucose Tolerance Reactions (Blood)					Urine	Remarks
					Fasting	½ Hour	1 Hour	2 Hours	3 Hours		
1	24	No	Hands	Red, crusted	111	155	142.5	118	91	Negative throughout	
2	70	—	Right leg	Varicose eczema	91	194	95	89	77	Negative throughout	
3	4	—	Genitalia	Dry, scaly	100	133	94	133	—	Negative throughout	
4	71	—	Arms, leg, back	Dry, scaly	122	167	121	111	82	Trace of sugar, 1 hr., 2 hr. ..	Kidney trouble, no details
5	37	Yes	Face, neck	Dry, thickened	110	127	108	83	80	Trace of sugar, 1, 2, 3 hr.	
6	67	—	Face, chest, neck, ankle	Dry, lichenified	121	100	118	114	69	Negative throughout	
7	50	—	Knee, knuckle	Dry, scaly	111	153	142.5	127	105	Negative throughout	
8	26	—	Hands	Dry, scaly	95	121	111	102	96	Not recorded	
9	65	—	Legs, anterior	Papular, oozing	99	167	159	113	77	Negative throughout	Hypertension
10	40	—	Neck, ears, face	Vesicular, papular	92	174	105	100	95	Negative throughout	
11	40	—	Shins	Raw, bleeding	100	180	111	108	72	Negative throughout	
12	4	—	General	Oozing	80	—	100	125	—	Trace of sugar, 2 hr.	
13	46	—	Fingers, knees	Vesicular	93	118	110	121	111	Negative throughout	Stomach trouble, chronic constipation
14	23	—	Arms, legs	Dry, papular	95	155	116	114	71	Negative throughout	Followed treatment for scabies
15	44	—	Neck (sides and front)	Papular	87	69	95	84	—	0.8%, 1 hr.	
16	62	—	Knees, thighs, arms	Papular, crusted	85	93	95	90	85	Negative throughout	Constipation
17	46	—	Neck, knee	Papular	125	182	161	155	145	Negative throughout	
18	48	—	Axillae	Papular, scaling	142.5	263	364	263	182	Trace of sugar, 1, 2 hr.	
19	40	—	Face, chest, arms	Excoriated papules	118	210.5	167	160	92	Trace of sugar, ½, 1, 2, 3 hr.	
20	32	—	Face, flexor surface right arm	Papular	125	182	155	142.5	89	Sugar, 0.7% 1 hr., 0.34% 2 hr.	
21	78	—	Arms, face	Papular (recurrent summer)	101.5	200	185	188	123	Negative throughout	
22	35	—	Neck, arms, chest, legs	Not recorded	100	155	177	145	118	Sugar, + 1, 2, 3 hr	
23	77	—	Legs, hands, arms	Erythematous	105	155	190.5	167	142.5	Sugar, trace 3 hr.	
24	51	—	Fingers, hands	Thickened	132	125	103	182	113	Negative throughout	
25	45	—	Feet	Not recorded	172	190.5	167	142.5	115	Negative throughout	
26	42	—	Right hand	Crusted	122	222	250	171	103	Sugar, trace 2, 3 hr.	
27	—	No	Hands, fingers	Dry, scaly	87	202	222	121	85	Negative throughout	
28	63	—	Face, hands	Dry, scaly	106	225	208	202	84	Sugar, trace 2 hr.	Rheumatism
29	27	—	Face, neck	Erythematous	80	182	192	103	93	Sugar, trace 2 hr.	
30	79	—	Legs	Dry	155	210.5	364	339	118	Sugar, 0.38% 1 hr., 0.55% 2 hr., 0.23% 3 hr.	Vesicular near borders; nocturia, 2 times
31	51	—	Fingers	Dry, scaly	89	174	214	139	131	Negative throughout	
32	40	No	Face, neck	Erythematous	103	125	167	121	106	Sugar, trace ½, 1 hr., + 2, 3 hr.	
33	53	—	Not recorded	Crusted, scaly	113	194	298.5	222	143	Sugar, trace ½ hr., 1 hr., + 2, 3 hr.	
34	40	—	General	Vesicular, oozing	120	167	117	116	123	Sugar, trace 2, 3 hr.	
35	47	—	Face	Dry	103	202	141	98	68	Negative throughout	Asthma and chronic constipation
36	16	—	Hand	Papular, crusted	125	250	182	125	125	Negative throughout	

37	10	—	Hands (dorsal)	Dry, scaly	98	160	172	333	—	Sugar, trace 1, 2 hr.	
38	59	—	Fingers, palms	Dry, fissured, thickened	108	108.5	101.5	112	142.5	Sugar, trace 3 hr.	
39	69	—	Neck, arms	Dry	95	114	112	96	—	Negative throughout	Asthma 35 years, epigastric pains past two weeks
40	70	Moderate	General	Dry, chafed	93	149	118	114	83	Negative throughout	
41	12	No	Trunk, forehead, fingers	Oozing, crusting	95	100.5	142.5	105	104	Sugar, + 1, 2 hr.	Allergic tests positive
42	29	No	Face, hands, axillae	Oozing, scaling	118	142.5	105	105	75	Negative throughout	
43	53	No	General	Papule, vesicular, oozing	112	148	194	114	82	Sugar, trace 3 hr.	
44	63	—	Hands	Vesicular	119	194	220	132	142.5	Sugar, 0.34% 1 hr., 0.4% 2 hr., 0.15% 3 hr.	Entirely free since having low carbohydrate diet
45	33	No	Left hand (dorsum)	Edema, confluent vesicles	100	160	155	142.5	87	Negative throughout	
46	25	—	Hands, arms	Vesicular	121	192	222	129	118	Negative throughout	
47	17	Yes	Hands, arms, thighs	Oozing, yellow crusts	105	129	133	128	121	Sugar, trace 1, 2, 3 hr.	Bought mah jongg set with lacquer box prior to onset
48	26	Yes	Face, neck, scalp	Edema, crusting	100	200	167	83	69	Sugar, trace ½, 1 hr.	
49	71	No	Right calf	Crusted, oozing	95	157	200	174	125	Sugar, trace 1, 2, 3 hr.	Varicose veins with swelling for 5 years
50	20	Yes	Palms, soles	Edema, large vesicles	114	222	200	121	91	Negative throughout	Urticaria and hay-fever, 11 food tests negative; no fungi
51	10	Yes	Thighs, popliteal areas	Thickened, crusted, excoriated	108	187	150	148	144	Negative throughout	
52	28	—	Hands, fingers (dorsum)	Dry, scaly, fissured	83	146	155	124	123	Sugar, trace 2, 3 hr.	
53	63	No	Right knee (flexual)	Thickened, excoriated	91	200	167	116	67	Sugar, trace 2, 3 hr.	Varicose veins many years
54	39	No	General, esp. face, neck	Scaling, crusting, thickening	94	133	167	107.5	75	Sugar, + 1 hr., trace, 2 hr.	Urticaria and hay-fever; abdominal pain 3 days prior to attack; 41 allergens negative, 1 positive
55	74	No	General	Dry, chafed	95	118	116	114	115	Negative throughout	3 or 4 baths daily, using soap
56	36	Yes	Forehead, eyelids	Dry, scaly, puffed	123	133	83	76	91	Negative throughout	Wore new tan wool scarf at onset
57	32	Yes	Thighs, knees, legs, hands, arms	Dry, thickened, excoriated	103	122	118	100	97	Negative throughout	No other allergic history; two brothers have eczema
58	43	Moderate	Face	Dry, thickened	91	142.5	83	118	105	Negative throughout	Hay-fever, urticaria sensitive ragweed, slender ragweed and 11 vegetables; eczema, July to November
59	20	No	Hands, fingers (dorsum)	Scaly, crusted	102	116	117	103	80	Negative throughout	
60	38	Yes	Scrotum, popliteal area	Scaly, thickened, fissured	100	155	133	87	74	Sugar, trace ½ hr., 0.3% 1 hr.	
61	66	No	Hands, wrists, forearms	Edema, vesicles oozing	89	134	130	98.5	72	Negative throughout	Hay-fever and asthma past 30 years
62	21	—	Face, neck, arms	Papular	220	235	317	303	200	Negative throughout	
63	32	—	Face, hands	Papular	111	250	133	192	125	Negative throughout	
64	54	—	Hands	Not recorded	101	174	142.5	118	72	Negative throughout	
65	28	No	Hands, wrists, fingers	Scaling, crusting, vesicles	90	163	138	119	50	Negative throughout	

TABLE 1.—*Glucose Tolerance in Cases Studied by Author—(Continued)*

Case	Age	Sugar Excess in Diet	Distribution	Type	Glucose Tolerance Reactions (Blood) Fasting	½ Hour	1 Hour	2 Hours	3 Hours	Urine	Remarks
66	72	Moderate	Hands, forhead.....	Sl. vesicular, scaling....	104	137	156	114	113	Sugar, trace 1, 2, 3 hr.	
67	30	—	Peri-anal.....	Macerated, sharply defined	118	218	148	125	101	Sugar, 0.29% ½ hr., 0.77% 1 hr., trace 2 hr.	
68	42	—	Hands, arms, feet, ankles	Edema, oozing, crusting	108	—	206	182	—	Sugar, 0.95% 1, 2 hr.	15 boils on abdomen 8 months ago; hands and arms exposed to water and steam
69	61	No	Hands, fingers.....	Vesicles, oozing, crusting	105	—	206	143	—	Negative throughout	
70	21	Yes	Forehead.....	Oozing, crusting.....	93	—	149	164	—	Negative throughout.....	Eczema in infancy, chronic constipation, intestinal fermentation
71	61	No	Legs, ankles, feet.....	Vesicles.....	151	186	250	296	244	Sugar, trace F., 0.33% 1 hr., 2.5% 2 hr., 4.1% 3 hr.	
72	36	—	Neck (sides).....	Vesicles, sl. blotchy.....	113	182	146	118	129	Sugar, 0.6% ½ hr., 0.4% 1 hr., trace 2, 3 hr.	
73	31	Yes	Face, neck.....	Blotchy, sl. vesicles.....	98	—	139	167	114	Sugar, trace 1 hr.	Psoriasis for 17 years, each 4 pregnancies disappearing between
74	29	No	Hands, wrists.....	Large vesicles.....	121	222	234	141	69	Sugar, 0.52% 1 hr., 0.65% 2 hr., 0.24% 3 hr.	
75	48	?	General.....	?.....	100	220	286	114	83	Sugar, 1.4% 1 hr., 0.24% 2 hr., trace 3 hr.	
76	45	No	Genitals (f.) breasts...	Edema, occ. vesicles....	104	166	238	259	190	Negative throughout	
77	11	Yes	Flexures elbows.....	Dry, scaly, excoriated..	100	232	182	121	68	Negative throughout	
78	60	?	Flexures arms, legs....	Chafed.....	200	294	334	344	250	Sugar, trace F., 5.5% 1 hr., 4.1% 2 hr., 4.3% 3 hr.	
79	48	Yes	Face, eyelids, flexure thighs	Crusted, chafed.....	105	—	222	100	—	Sugar, trace 2 hr.	Hay-fever past 10 years, June to August; 7 pollen allergens negative
80	36	No	Palms, fingers.....	Dry, scaling, thickening	121	242	216	160	80	Sugar, trace F., 0.3% ½ hr., 3.8% 1 hr., 2.2% 2 hr., 0.8% 3 hr.	Followed scalding of hand
81	48	Yes	Hand, fingers, chin, eyelids, neck	Dry, scaly, chafed.....	107	—	286	210	—	Sugar, trace 1, 2 hr.	
82	56	Yes	Dorsum hands.....	Dry, scaly, chafed.....	127	170	138	133	111	Sugar, 0.2% 2 hr., 0.21% 3 hr.	
83	40	No	Palms, ankles, perianal	Thickened, crusted.....	100	210	212	100	138	Negative throughout	
84	83	—	Hands (backs), neck...	Dry, scaly, fissured.....	149	238	232	206	167	Sugar, 0.9% 3 hr.	
85	39	Yes	Hands (backs), arms, neck	Dry, scaly, chafed.....	82	122	112	112	67	Negative throughout	
86	35	Yes	Legs, arms (flexor and extensor)	Dry, diffuse, chafed.....	100	260	150	100	—	Negative throughout	

The tests were made in four different laboratories; the laboratory of Drs. Brem, Zeiler and Hammack, the Metabolic Research Clinic of the White Memorial Hospital under the direction of Dr. H. E. Butka, the laboratory of the Pasadena Hospital and the laboratory of Dr. G. F. Ruediger. All but three of the tests were made in the first two laboratories, and, of these, sixty-four were made at the White Memorial Hospital and nineteen at the laboratory of Brem, Zeiler and Hammack. All of the laboratories used the Folin-Wu [3] colorimetric technic, obtaining the blood by puncture of the vein. All the tests were made about fourteen hours after the last meal, and the test meal consisted of 1.75 gm. of glucose per kilogram of body weight [4] in about 300 c.c. of water, except in four cases, in which the test meal consisted of 100 gm. of glucose.

McGlasson's series consisted of 158 cases of assorted dermatoses, mostly of an eczematous type. Of the entire series, 139 cases, or 87.9 per cent., gave fasting values of 120 mg. or more of sugar, per one hundred cubic centimeters of blood. Between 90 and 100 mg. would probably be considered an average normal reading. All of McGlasson's determinations were made in one laboratory, using the Gradwohl gravimetric method in the majority of cases, although Gradwohl's modification of the Lewis-Benedict colorimetric method was used in many of the cases, and both methods were used simultaneously in many tests, with close agreement. McGlasson found that many of these patients improved rapidly on a low carbohydrate diet, even when no local treatment was applied.

The general impression given by McGlasson's work in regard to a disturbed carbohydrate metabolism in many cases of eczema is confirmed by the glucose tolerance reactions in this series of eighty-six cases, but the disturbance is not as prevalent in this series. Thus, while 87.9 per cent. of his cases gave fasting blood sugar values of 120 mg. or more per one hundred cubic centimeters, only 23.8 per cent. of this series gave corresponding fasting values. In fact, 30 cases, or 34.8 per cent., of these eighty-six cases, gave glucose tolerance reactions which would be considered entirely normal in every respect. Thirty-two cases, or 37.2 per cent., showed decidedly abnormal curves, leaving about 28 per cent. showing slight abnormalities. The cases showing definitely abnormal reactions were Cases 18, 23, 26, 27, 28, 30, 31, 33, 36, 37, 38, 44, 46, 50, 51, 62, 63, 67, 68, 70, 71, 73, 74, 75, 76, 77, 78, 80, 81, 84 and 86.

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3. Folin, O., and Wu, H.: A Simple and Improved Method for the Determination of Sugar, J. Biol. Chem. **41**:367 (March) 1920.

4. Janney, N. W., and Isaacson, V. I.: A Blood Sugar Tolerance Test, J. A. M. A. **70**:1131 (April 20) 1918.

According to John [5] the mere peak of the blood sugar content after the ingestion of glucose appears to have little or no significance, from the point of view of diabetes. The most important point is the length of time required for the reestablishment of the normal level after the ingestion of the glucose test meal. If the curve comes back to normal inside of three hours, the patient is considered nondiabetic; if after three hours, he is considered diabetic. In this series, however, both the height of the peak and the delayed return to normal are taken into consideration in classifying a reaction as "distinctly abnormal," although more weight is given to the delayed return to normal. Dividing the series, it is seen that of the nineteen cases tested at the Brem, Zeiler and Hammack laboratory, thirteen cases, or 68.4 per cent., gave decidedly abnormal reactions, while of the sixty-four cases tested at the White Memorial laboratory, only seventeen cases, or 26.5 per cent., were markedly abnormal. Both laboratories used the same method, and the procedures were carefully supervised in each instance. The degree of abnormality of the blood sugar was roughly parelleled in each series by the degree of abnormality of the sugar in the urine, thus confirming the accuracy of the tests, and showing the discrepancy in the two series to be due merely to the law of chance, unless the social condition of the patients might be of some influence.

The larger series was made up, for the most part, of clinic patients, who were in rather limited financial circumstances, while the smaller series consisted largely of patients in comfortable circumstances. As mentioned above, the tests were made as a matter of routine wherever possible, without any attempt at selection, so that the series includes cases both mild and severe, extensive and localized, chronic and acute, oozing and dry.

Although the majority of the cases in this series showed little or no evidence of abnormality of their carbohydrate metabolism as revealed by the glucose tolerance test, nevertheless, the important fact remains that a little more than one fourth of them were decidedly abnormal, The fact that none of these abnormal patients had ever suspected any derangement of their mechanism for the utilization of carbohydrate, and that eczema was the cardinal symptom which led to the discovery of their decreased sugar tolerance, deserves recognition from the point of view of preventive medicine. None of these distinctly abnormal patients could be considered as having severe diabetes; several of them had mild diabetes, but showed sugar-free urine in a few days on a modified diabetic diet, and the eczema cleared promptly; the others could possibly

5. John, H. J.: Glucose Tolerance and Its Value in Diagnosis, J. Metabolic Res. **1**:497 (April) 1922.

be classed as being in a prediabetic condition. The use of insulin was not required in any case. At the present time, it cannot be said that the disturbed carbohydrate metabolism is the cause of the eczema; it may be merely associated, and may be due to some more fundamental endocrine disturbance. At any rate, the carbohydrate tolerance must hereafter be given serious consideration in the intelligent treatment of any given case of eczema. There are, of course, many cases of eczema in which there is no disturbance in carbohydrate metabolism, and, in these cases, other abnormalities must be searched for, such as sensitization to certain food, pollen or epidermal proteins, gastro-intestinal disturbances of various sorts, nephritis, external irritants and no doubt some causes as yet unknown.

It does not seem rational to attempt to divide the cases in this series into separate groups, based on the clinical appearance at the time of examination, for many of them either gave a history of some previous eczematous attack, which represented a different phase, or else passed through one or more different manifestations while under observation. Since it is well recognized that an attack of eczema, in a given person, may pass through many phases during a few weeks or months, it is difficult to see what advantage could be gained by making such artificial differentiations.

A seriously disturbed carbohydrate metabolism does not seem to be associated with any one particular clinical type of eczema. Thus Cases 71 and 78, in both of which there were abnormal glucose tolerance reactions amounting virtually to a mild diabetes, represent exactly opposite clinical types of eczema, Case 71 showing lesions, profusely vesicular, oozing and crusted; while Case 78 presented dry, erythematous, chafed-looking areas. Localized types are just as likely to be associated with decreased sugar tolerance as generalized types; Case 55, in which the condition was generalized, and Case 45, in which it was localized to one hand, showed normal curves, while Case 75, in which the condition was generalized, and Case 26, in which it was localized to one hand, showed distinctly abnormal curves.

Notes were made of other allergic manifestations in nine cases, although it is possible that this condition may have been more prevalent than the notes would indicate. Of the nine cases, urticaria occurred in five, hay-fever in five and asthma in three, several showing more than one type of allergic reaction. Three of the nine, or thirty-three per cent., gave markedly abnormal glucose tolerance curves. In the only three cases in which positive food or pollen sensitization tests were made, the glucose tolerance reactions were normal. It would be interesting to know whether, in a larger series of cases, there would be any relation between allergic conditions, such as allergic eczema, urticaria,

angioneurotic edema, hay-fever and asthma on the one hand, and disturbances in carbohydrate metabolism on the other hand, of if they represent entirely different types of disorder. No conclusions can be drawn from the nine cases in this series showing allergic tendencies.

The average age of those tested who showed markedly abnormal reactions was 42.4 years; 31 per cent. were 30 years of age or under. No infants were tested.

In order to appreciate the extent of the abnormality in the glucose tolerance reactions in some of these cases of eczema, it is necessary to consider the type of curve given by a clinically normal person, and to determine the range of variation which would be considered within normal limits. The large series of tests made on clinically normal persons reported by Horace Gray [6] has been used as the standard of

TABLE 2.—*Comparison of Glucose Tolerance in Persons with Eczema and Normal Persons*

No. of Cases	Time	Range	Average
		Normal Series	
276	Fasting	40 to 160 mg. per 100 c.c., 2 above 130	91.5
158	½ hour	60 to 230 mg. per 100 c.c., 5 above 200	144.0
300	1 hour	40 to 280 mg. per 100 c.c., 5 above 200	121.0
253	2 hours	30 to 260 mg. per 100 c.c., 2 above 160	105.0
103	3 hours	40 to 170 mg. per 100 c.c., 1 above 140	94.0
		Eczema Series	
86	Fasting	80 to 220 mg. per 100 c.c., 8 above 130	109.0
79	½ hour	69 to 294 mg. per 100 c.c., 20 above 200	173.0
86	1 hour	83 to 364 mg. per 100 c.c., 22 above 200	168.0
86	2 hours	76 to 344 mg. per 100 c.c., 20 above 160	142.0
75	3 hours	67 to 250 mg. per 100 c.c., 12 above 140	107.5

comparison. The reports of these tests were collected from recent literature and represent the results obtained by numerous investigators using various modern standard technics.

The series comprises 276 tests made at the fasting period, 158 tests at the half hour interval after the taking of glucose, 300 tests at the one hour interval, 253 tests at the two hour interval and 103 tests at the three hour interval.

A comparison of the range of values for the different periods with the average for each period in the series of normal controls and the eczema series is given in Table 2.

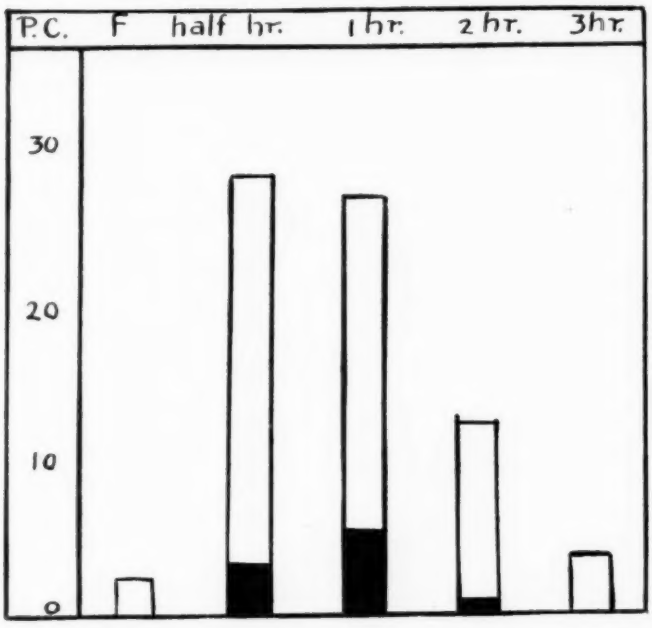
Figure 1 illustrates the frequency of extreme deviation from normal among the eczema cases as contrasted with the control series. The percentage of cases in each series showing values of 200 mg. or more at each period is charted.

6. Gray, Horace: Blood Sugar Standards, Arch. Int. Med. **31**:241 (Feb.) 1923.

Curves representing the average values in each series, and the curves of two cases of eczema showing markedly decreased glucose tolerance are shown in Figure 2. The two cases the reactions of which are plotted in the diagram are worthy of detailed description.

REPORT OF CASES

CASE 71.—*History.*—E. F., a railroad brakeman, aged 63, was seen for the first time about two years before, when he had a diffuse, red vesicular, crusted eruption of both legs and ankles, which had been present for about ten months.



ECZEMA	2.3	29	27.9	12.7	4
NORMAL	0	3.8	5.6	.8	0

Chart 1.—Percentage of cases showing values of 200 mg. or more of sugar per hundred cubic centimeters of blood at the different periods.

The trouble first appeared on the backs of both hands about two years prior to his first visit and remained localized for about fourteen months, then disappeared from the hands and has been on the legs and ankles since. He had had attacks of urticaria over a long period of time, but none for the last four or five years. He had had hay-fever for many years, usually from June to October or November; the eczema seemed to be better during the attacks of hay-fever. There was no history of an excessive use of sugar, but a moderate amount was consumed in coffee, pie, doughnuts, etc. He said that he ate little meat. The bowels usually moved twice daily without laxatives;

he had been troubled with considerable gas in the lower bowel and loose, floating, unformed stools. The bowel condition improved very much under the administration by mouth of fresh cultures of *Bacillus acidophilus* for a month. He complained of a loss of sexual potency during the last eight years, although desire was still present. During the last three years he had had nocturia, usually three or four times a night. He was always thirsty and drank much water.

Laboratory Examination.—This revealed a negative Wassermann reaction. Routine blood test revealed hemoglobin, 100 per cent.; red cells, 5,368,000; white cells, 6,600; smear: polymorphonuclears, 65 per cent.; lymphocytes, 32.5 per cent.; large mononuclears, 1 per cent.; eosinophils, 1.5 per cent.; no abnormal forms were seen. Urine was negative for albumin and sugar (Benedict's test). Thirteen food allergen tests gave negative results. Blood sugar (fasting) was 189 mg. per cubic centimeter of blood, and the uric acid was 3.4 mg. per cubic centimeter of blood. A glucose tolerance test gave the following reaction: fasting, 100; in one hour, 286, and in two hours, 236. The urine at the fasting and one hour periods was negative for sugar; at two hours, 0.71 per cent. of sugar was present.

Treatment and Course.—The patient was placed on a diabetic diet and improved for a time, but frequently overstepped his diet and ate pie or coffee sweetened with sugar. The eczema varied during a period of observation covering about two years. For several months at a time, he would be practically free; again the eruption would break out afresh, with oozing and crusting. At one time, he developed a moderately itchy eruption of both thighs, extending up onto the buttocks. The eruption consisted of dry, slightly scaly macules, many of which were excoriated; some were arranged in hollow circles and other bizarre designs, strongly suggestive of a prefungoid eruption of mycosis fungoides. The eruption subsided within a week or two.

About two years after the first visit, the patient had a severe attack of eczema of the legs, ankles and feet, with a vesicular eruption on the soles, which later became infected and superficially ulcerated necessitating hospitalization. Microscopic examination of sections of the vesicles failed to reveal any fungi. A second glucose tolerance test, made by the same laboratory (B. Z. H.) seven months after the first one revealed an even more pronounced abnormality with a fasting value of 151; after one-half hour, 186; one hour, 250; two hours, 296, and three hours, 244. The urine showed a trace of sugar at fasting, no specimen was obtained at the half hour; 0.33 per cent. at one hour; 2.5 per cent. at two hours and 4.1 per cent. at three hours.

The patient was again placed on a strict diet and advised as to a possible serious outcome from failure to cooperate. He has followed instructions, eliminating all sugar, and for two months, up to the present writing, has remained entirely free from eczema. Local applications were used to clear up the recent acute attack.

Case 78.—W. H. H. was a man aged 69. The eruption had been present about eighteen days, having begun while the patient was on the train en route from New York to Los Angeles. There was no history of any previous skin trouble or of allergic manifestations, and the patient considered himself in good health. He had had a tonsillectomy about three months before. He had used no soap on the body for the past two weeks.

The entire cutaneous surface was dry. The eruption was rather diffuse, but occurred for the most part on the medial aspect of the legs, knees and

thighs, and on the flexual and medial surfaces of the forearms. The lesions consisted of diffuse red, chafed-looking areas. There were no vesicles or crusting.

Examination of urine passed at the time of his visit revealed no albumin, but a heavy qualitative test for sugar (Benedict's). The glucose tolerance reaction showed the following: fasting, 200; one-half hour, 294; one hour, 334; two hours, 344, and three hours, 250. The urine showed a trace of sugar at fasting, no specimen at one-half hour; 5.5 per cent. at one hour and forty-five

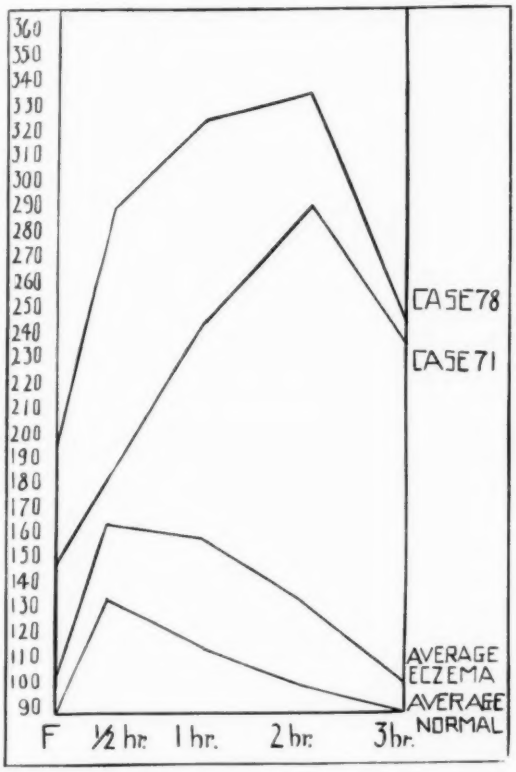


Chart 2.—Average curves of the eczema and the normal group with two distinctly abnormal curves.

minutes; 4.1 per cent. at two hours, and 4.3 per cent. at three hours. The patient was given a soothing shake lotion and placed on a diabetic diet. The skin condition cleared promptly and has not recurred during the past four months.

Comment.—The interpretation of the findings in this rather small series of cases must be approached with the utmost caution. The significance of an abnormal glucose tolerance reaction in eczema is not clear. Does it point to a beginning diabetes, in other words, a deficiency

of the pancreatic internal secretion? Does it indicate a deranged endocrine function of unknown type, possibly involving the thyroid or the pituitary? Or does it mean a deficient liver function? The answer cannot even be attempted in our present state of ignorance.

Further investigations into the metabolic, endocrine and chemical processes of the body may throw light on a problem which at present seems hopelessly obscure. Observed facts justify the statement that an appreciable percentage of cases of eczema are in some way associated with a disturbed carbohydrate metabolism, at least as revealed by the glucose tolerance test, and that many of these cases show clinical improvement following a reduction of the carbohydrate intake. Other etiologic factors must not be lost sight of, such as allergy or protein hypersensitiveness. Subsequent investigations may synthesize many isolated facts and present a unified picture, or we may learn that there are many unrelated causes of eczema, each of which must be carefully searched for once the diagnosis is made.

The purpose of this paper is the presentation of certain facts. It is hoped that others will add to them, and that their interpretation will be forthcoming as our knowledge increases.

SUMMARY

1. A report is presented dealing with the glucose tolerance reactions in a series of eighty-six consecutive cases of typical eczema.

2. The tests were about equally divided between two laboratories, each using the Folin-Wu colorimetric technic. A few tests were made in two other laboratories, but the results of all four laboratories were in general agreement.

3. The average values of the entire series of cases at the fasting, half hour, one hour, two hour and three hour periods were all distinctly higher than the average values at corresponding periods in a large series of clinically normal persons.

4. A normal fasting blood sugar value does not prove that a given case of eczema is not of the hyperglycemic type, since many cases showing markedly decreased tolerance reactions had perfectly normal fasting values.

5. In this series of eighty-six cases, there is no constant association of decreased sugar tolerance with any one definite clinical type of eczema.

6. The percentage of cases in the eczema group showing unusually high values was much greater than in the normal group. Thus, in the eczema group, 12.7 per cent. of the eighty-six cases showed readings of 200 mg. or more of sugar per one hundred cubic centimeters of blood

two hours after the test meal, as compared with 0.8 per cent. of 253 clinically normal persons.

In other words, there were more than fifteen times as many decidedly abnormal reactions in the eczema series as in the normal series at the two hour interval.

7. In not a single instance in which an abnormal reaction was present had the patient been aware of the existence of any disturbance of his carbohydrate metabolism.

DISCUSSION

Dr. I. L. McGlasson, San Antonio, Texas: I appreciate very much Dr. Ayres' work along this line, and feel that it is in line with the modern trend of dermatology. Particularly do I appreciate his work because it more or less completes my attempt in the paper quoted by him. I have made some tolerance tests in indicated cases, but not as a routine, and am submitting two tests which are very interesting, particularly a case in which the constant blood sugar finding was above 0.15, in which there was a recurrence, and the patient still showed a negative urinalysis. The tolerance test showed 0.21; in one half hour, 0.2, and in one hour, 0.38. The sugar curve in that case was so unusual that I could not get a satisfactory explanation. An interesting feature of this case is that despite the high sugar findings, the urine was continuously negative and, secondly, the sugar curve was not materially affected by insulin, except on one occasion when we had an insulin shock. The difference in Dr. Ayres' findings may be due to the fact that his were routine examinations, while mine were made in selected cases. I realize that my classification was an arbitrary one, but still believe that there are types which will show a higher percentage of hyperglycemia than will other types, and I am not speaking of the cutaneous manifestations ordinarily found in diabetes. I would not attempt to prove, nor do I believe, that hyperglycemia is a constant finding in any particular type of eczema, but I do believe that in certain types it is of sufficient importance to justify investigation in all cases in which a definite etiologic factor, either external or internal, is not shown, and it is an aid in those types that are very resistant to treatment. Certainly when hyperglycemia is found, correction of this condition is indicated, and the therapeutic benefit is so marked in the majority of cases that this procedure is worth while.

I also believe it is of value as an addition to our armamentarium along the lines of preventive medicine. The work at present does not admit of a positive statement that a given case is prediabetic, but it is not believed possible that a high blood sugar content could continue for any great length of time without a spill-over in the kidney.

Dr. Ayres has made a valuable contribution to this work in his comparison between the normal and the eczema series. I fail to see how these findings can do other than prove that carbohydrate metabolism is frankly disturbed in some cases of eczema. His fourth conclusion has been repeatedly proved clinically by the fact that in cases with a normal fasting, blood sugar values are in many instances markedly improved on a carbohydrate-free diet.

All this work is simply a contribution to the unknown etiology of eczematoid eruption. I hope that more dermatologists will become interested in this subject and that we will be able to present some definite facts, such as carbohydrate dis-

turbances in eczema, which will be an additional contribution by dermatology to scientific medicine.

I just wish to add that recently we have adopted the Folin test, and all of our work is based on that at present.

Dr. Karl G. Zwick, Cincinnati: Therapeutic diagnostic tests are not particularly accurate, as we know from various experiences, but the other day I asked an internist whether he thought it would be safe to try small doses of insulin in cases of eczema of indefinite etiology. He seemed to think this procedure would be justifiable as a diagnostic measure in doses of one to three units.

Dr. Jeffrey C. Michael, Houston, Texas: This is an interesting subject. Of course, for a long time it has been known that diabetes was associated with various skin disturbances, but it is only since blood sugar studies have been made that a prediabetic state has been shown to be an etiologic factor in certain skin diseases.

We are now working with instruments of precision and are able to pick up these cases in an early stage where hitherto we had to wait for more gross manifestations. In investigations of this sort, I believe we should fix on some standard method, and I suggest the Folin-Wu as the method of choice.

My own experience has been similar to Dr. Ayres'. There is an appreciable but small percentage of cases of eczema that show lowered glucose tolerance. These cases do not fall into any particular type, but apparently any type of eczema may be associated with a prediabetic state.

Dr. William Allen Pusey, Chicago: I think a word of appreciation should be expressed for the attention that has been called to this aspect of eczema by Dr. McGlasson and Dr. Ayres. It is not necessary to tell us that there are some cases of eczema perhaps of unknown origin. I should leave out the "perhaps" and emphasize the "some." It is a valuable service to call our attention to this factor in the etiology of eczema that has been overlooked. For that Dr. McGlasson deserves great credit, and I am glad that Dr. Ayres and Dr. Michael are pushing the work further. I am thoroughly convinced that there is a great deal of value in it, and I did not like to see the discussion simply on technical details without someone expressing appreciation of the work.

Dr. Samuel Ayres, Jr., Los Angeles: I realize, of course, that disturbance in sugar metabolism as a cause of eczema is not new. It has been recognized for many years, but it is not dwelt on. Few of the textbooks on dermatology stress the idea, and it seemed worth following up. I am indebted to Dr. McGlasson for starting it going.

In regard to the urinary findings, quite a number of cases showed sugar in the urine in the active stage, some cases as much as 2 or 3 per cent.

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STUDIES ON HAIR

WITH SPECIAL REFERENCE TO HYPERTRICHOSIS

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II. THE HAIR OF MAMMALS

All kinds of mammalian hair have sufficient similarity to justify the belief that they have had a common phylogenetic origin. Whether hairs were originally protective or sensory has frequently been discussed, but there is considerable likelihood that at first they were neither wholly the one nor the other. Among living mammals, the protective function of hair is obvious, and at the same time there can be no doubt that many hairs, particularly the highly specialized tactile ones, play an important rôle in sense perception. The wide gaps that exist, for example, between movable sensory hairs and fine down or coarse spines are bridged by intermediate forms. That one or another of the various types of hair represents the persistence of an unmodified remnant from the covering of an early mammalian prototype, is not supported by adequate evidence. In the light of what knowledge we have, it seems more probable that the earliest mammals, or their immediate ancestors, possessed cutaneous appendages related to the integumentary organs of several other classes of vertebrates, but having in generalized form many of the characteristics of hair as we now know it. From some such primitive hair, it may be presumed that the more or less diversified types which we find today have been evolved, sometimes side by side in the same line of descent, sometimes in different lines.

DEVELOPMENT OF HAIR

Hairs are essentially highly specialized epidermal outgrowths, characterized by marked keratinization, and usually containing pigment considerably in excess of that found in the surrounding unmodified epithelium. So far as embryologic studies have been able to determine, their development generally begins with a thickening of the ectoderm, followed by a modification of the subjacent mesenchyme (Figs. 3 and 4). The ectodermal thickening grows obliquely downward and, for the most part, forward, to a depth roughly proportional to the size of the hair to be produced. Its basal portion gives rise to the hair bulb, the remaining portion to the epithelial part of the follicle and to the accessory glands. The mesenchyme forms a papilla projecting into the end of the hair bulb, the surrounding connective tissue part of the hair

follicle and the arrector pili muscles. According to Fibroes, it also contributes collagenous fibers to the formation of the hair itself. In a few cases (e. g., specialized quills of the European hedgehog and sensory hairs of the sheep), it has been reported that future hairs are foreshadowed by concentrations of mesenchymal nuclei which appear simultaneously with, or even preceding, the occurrence of ectodermal thickenings. This raises a question as to where development of the follicle is actually initiated, and whether or not it is always dependent on the same factors. Although this is an important consideration from the point of view of morphology of the hair, it has not yet been possible to settle the matter in a satisfactory manner.

The hair shaft is produced within the follicle by a multiplication of cells in the hair bulb. As these cells increase in number they are pushed upward in the core of the follicles, which in turn tends to disintegrate, forming a canal. At the same time, the young hair cells assume their definitive arrangement in the shaft and become cornified. Elongation of the shaft is effected through the continued addition of new cornified cells from below. After it is once well started, growth of the hair is generally more or less uniform and continuous until the definitive length has been nearly attained. At the beginning and toward the end of a growth period, the number of cells entering into the formation of the shaft for a unit of length is less than during the intermediate period, as indicated by the fact that nearly all hairs are pointed at their tips and, when full grown, narrowed toward the roots. While some hairs are, through the greater part of their length, approximately cylindrical, giving a circular cross section, deviations from this form are common, the most frequent involving a slight flattening of such nature as to give the hair an elliptical outline in cross section. The extreme deviation is met in the flat, bilaterally symmetrical hairs of *Ornithorhynchus.*

Since the hair follicle generally grows obliquely forward under the epidermis, the tip of the hair most commonly points backward or downward. But this is true only in a general way, since there are many variations and even reversals in the direction of the hair stream in different animals (Fig. 18). The direction of hair in mammals, including man, has been studied extensively by Walter Kidd, who sees in the hair stream an indication of physiologic response to such external factors as pressure and gravity. The supposed transmission of these acquired relations to the offspring he designates as "use inheritance."

When the hair has attained its full size, cells in the matrix of the bulb cease to divide, and the bulb itself becomes cornified. The connective tissue papilla partially atrophies, and a "resting" stage ensues, toward the end of which by multiplication of undifferentiated cells, the

hair bulb is pushed toward the surface. Ultimately a new bulb forms, possibly through proliferation from the "epithelial bed" in the side of the follicle, the connective tissue papilla regenerates, and another hair is developed. The old hair, if it has not already fallen, is generally crowded out by the new one. The duration of this cycle varies with different hairs and with different animals. In many cases a tendency for hairs of the same kind to pass through the cycle simultaneously is evidenced by seasonal moults.

STRUCTURE OF HAIR

A generalized hair in its follicle is represented in Figure 19. The hair shaft itself consists of cuticle, cortex and medulla, the latter frequently being absent. When the medulla is not present, its usual position is marked in a few instances by cavities extending for some

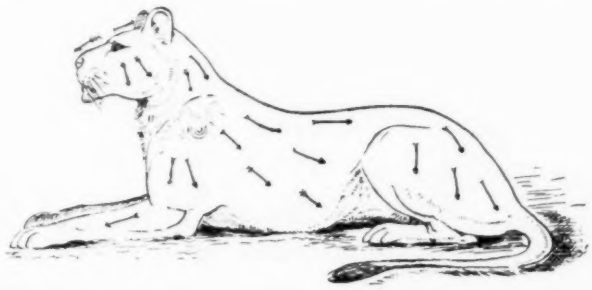

Fig.18.—A lioness, to show a relatively simple plan of hair arrangement (Kidd). Arrows with single barb represent the direction taken by hair that retains its presumed primitive arrangement; those with extra barbs indicate regions in which a change in direction has taken place.

distance along the shaft, but usually hairs without medulla have a solid cortical core. Rarely, if ever, does the medulla extend the full length of a hair. It is ordinarily absent for some distance back from the tip and frequently again near the root. In the shaft of the hair, the medulla may be interrupted for short distances, through which the hair consists of cuticle and cortex alone.

The cuticle is a thin, unpigmented layer composed of more or less overlapping scales whose free margins are directed toward the tip of the hair. Within the follicles these scales interlock with the cuticle of the inner hair sheath, the scales of which point in the opposite direction and thus help to hold the hair securely in place. In general, cuticular scales are relatively smaller in coarse hairs. Even in the same hair, an inverse relation between the size of the scales and the diameter of the shaft is often apparent in passing from one end of the hair to the other. Two hairs standing side by side but of different size may show

a marked difference in the character of their scales. Nevertheless, while the form of the scale may be considerably influenced by the size of the hair shaft and possibly of other mechanical factors, there are characteristic specific differences, as Hausman has pointed out in a recent series of articles. In some cases, each scale completely surrounds the hair, the successive scales fitting over each other like a series of hollow

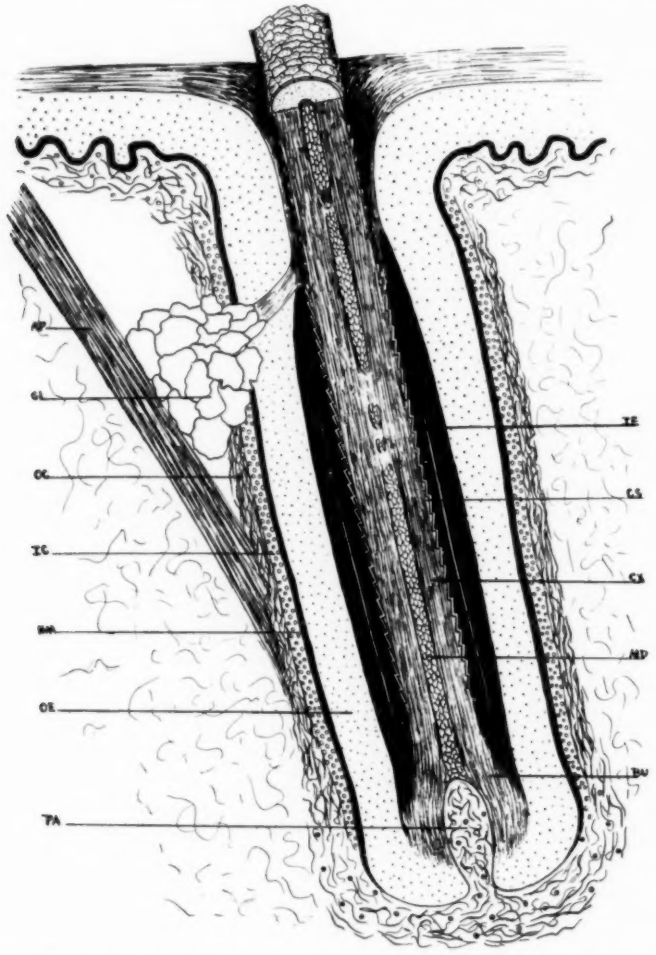

Fig. 19.—Diagram of a hair in its follicle. The follicle and the part of the hair beneath the surface are split longitudinally. Contacts between adjacent layers are suggested. *AP*, arrector pili muscle; *GL*, a sebaceous gland; *OC*, longitudinal fibers of the connective tissue sheath; *IC*, circular fibers of connective tissue sheath; *HM*, hyaline membrane; *OE*, outer epithelial sheath; *PA*, hair papilla; *IE*, internal epithelial sheath, divided through part of its extent into outer (Henle's) and inner (Huxley's) layers, the latter with cornified scales which articulate with those of the hair cuticle; *CS*, cuticular scales of the hair shaft; *CX*, cortex of the hair; *MD*, medulla of the hair.

truncated cones; but more frequently individual scales do not reach all the way around the hair shaft, in which case they are imbricated in a manner not unlike the arrangement of scales on a fish. The genetic relations of the several classes of scales is a matter that needs further study. The following classification is that employed by Hausman, and the accompanying illustrations are from his papers.

CLASSIFICATION OF CUTICULAR SCALES

1. *Imbricate.*—Individual scales not completely surrounding the shaft, classified according to the free margin as: ovate (Figs. 20 and 21; *a* and *i*), acuminate (*b*), elongate (*c*), crenate (*d*) and flattened (*e*).
2. *Coronal.*—Individual scales completely encircling the hair shaft, classified according to the free margin as: simple (*f*), serrate (*g*) and dentate (*h*).

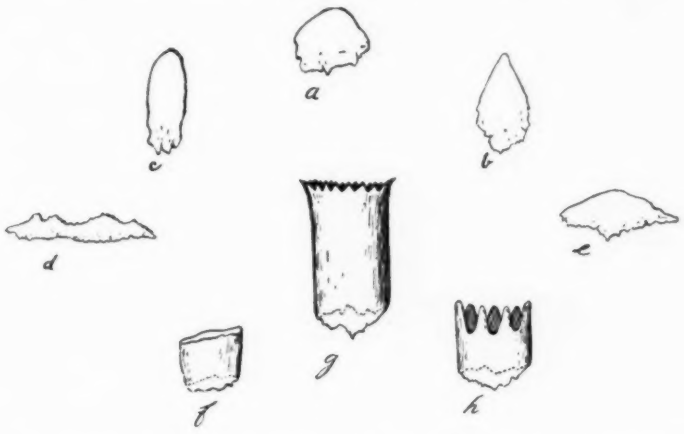

Fig. 20.—Types of cuticular scales. (After Hausman.) *a-c*, imbricate; *f-h*, coronal; *a*, ovate; *b*, acuminate; *c*, elongate; *d*, crenate; *e*, flattened; *f*, simple; *g*, serrate; *h*, dentate.

The cortex, constituting the main body of the hair shaft, is composed essentially of compact keratinized cells which have been compared to those of the stratum corneum of the skin. When isolated, these cells are found to be for the most part fusiform or elongated. According to Friboes, they are intermingled with fibers of connective tissue origin. The cornification is so complete that in the absence of pigment the cortex is usually translucent to a marked degree. Pigment, however, is commonly present, appearing in several forms that, according to Gortner, may probable be grouped in two general classes, the melanoproteins, which are acid-soluble, diffuse and nongranular, and the acid-insoluble melanins, which appear in the form of definite granules. Either one or both may be present in a given hair, but the granular form is not often lacking.

The medulla is far less dense than the cortex. Its cells are fewer, larger and more loosely held together. Pigment is often present. As a rule, among the medullary cells there are real or virtual spaces filled by replaceable gas, probably in most cases air. Such spaces are not often directly demonstrable except by optical effects, but in a favorable specimen it is easy to watch a film of fluid make its way along the medulla of a hair placed in a suitable solution under the lens. The medullary cells

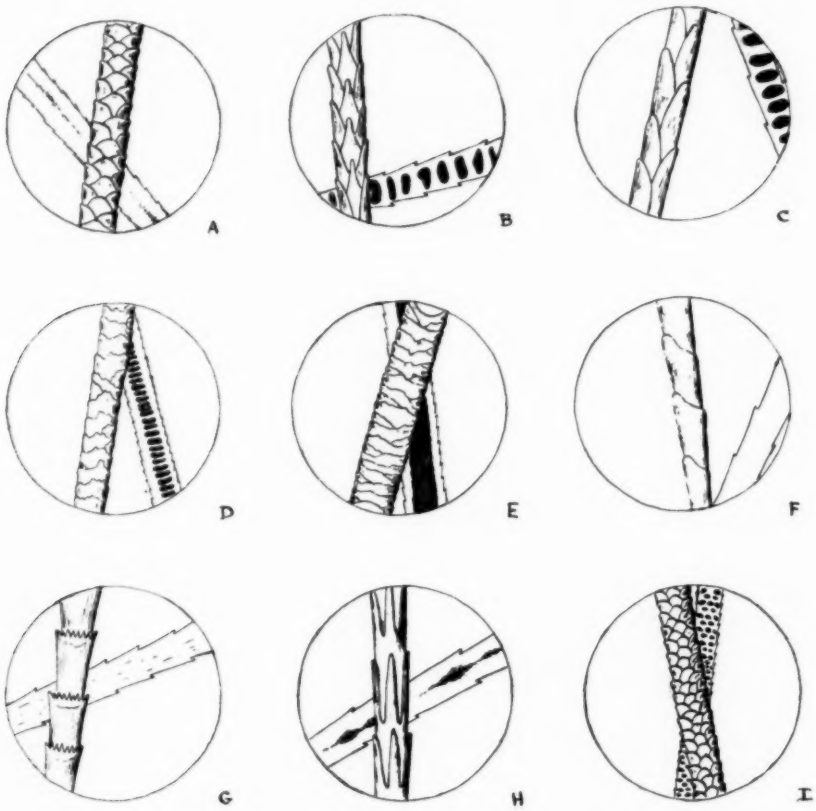

Fig. 21.—Representative mammalian hairs. (After Hausman.) In each circle one hair is shown in surface view, the other in optical section. The magnifications are not all the same. *A*, civet, showing ovate imbricate scales and a medulla apparently on the borderline between continuous and fragmental; *B*, star-nosed mole, scales acuminate imbricate, medulla discontinuous and intermediate between ovate and flattened; *C*, golden mole, scales elongate imbricate, medulla ovate discontinuous; *D*, camel, scales crenate imbricate, medulla flattened discontinuous; *E*, Tragulus, scales flattened imbricate, medulla nodose (?) continuous; *F*, Porto Rican bat, scales simple coronal, medulla lacking; *G*, intermediate bat, scales serrate coronal; *H*, European otter, scales dentate coronal, medulla elongate discontinuous (?); *I*, kangaroo rat, scales ovate imbricate, medulla of the ovate, compound discontinuous type.

proper tend to be grouped along the central axis of the hair, where they may form either a continuous or an interrupted core. In some cases, there may be several parallel or anastomosing and mostly discontinuous columns of medullary substance. In such instances, there need be no medulla in the actual center of the hair. The classification employed by Hausman in dealing with fur hair is essentially as follows:

CLASSIFICATION OF MEDULLAS IN FUR HAIR

1. *Discontinuous.*—Medullary cells in discrete groups separated by "interstitial medullary spaces."
    1. Simple: Groups of medullary cells in a single column. Depending on the ratio of the longitudinal to the transverse diameter of the masses, they may be: (*a*) ovate (Fig. 21, *C*), (*b*) elongate, (*c*) flattened (Fig. 21, *D*).
    2. Compound: Groups of medullary cells in two or more columns: (*a*) ovate (Fig. 21, *I*), (*b*) flattened.
2. *Continuous.*—Medullary column continuous (characteristic of spines, bristles, most other coarse and many finer hairs).
    1. Homogeneous: Diameter of the medullary column more or less uniform except at the ends, where it may taper.
    2. Nodose: Diameter of the column variable, giving a somewhat moniliform appearance to the medulla as a whole.
3. *Fragmental.*—Medulla interrupted irregularly, differing in this respect from discontinuous types of medullas where the "medullary chambers" are regularly disposed.

Hausman makes the suggestion that the evolution of the medulla is "from the discontinuous through the continuous to the fragmental and finally . . . to no medulla at all."

The hair follicle (Fig. 19), as already indicated, consists of elements of ectodermal and of mesodermal derivation. The former closely surrounds the hair from the bulb nearly to the point of exit from the skin, and may be subdivided into an inner and an outer epithelial sheath, both of which are more or less continuous above and below. The outer epithelial sheath rests on a hyaline membrane, and is composed of cells which are comparable to those of the stratum germinativum in unmodified epithelium. The inner epithelial sheath is immediately surrounded by the outer, from which it is not always clearly distinguishable. Toward the bottom of the follicle, it may be subdivided into two concentric laminae, the outer being designated as Henle's layer, the inner as Huxley's layer. Resting on Huxley's layer and immediately in contact with the hair is a thin cuticle composed of scales, whose free margins point downward and interdigitate with those of the hair cuticle.

No wholly satisfactory comparison between the epithelial layers of the follicle and the surface epithelium has been made, but it has been

pointed out that if the skin were stretched so that the hair bulb would be brought to the surface and the follicle spread out flat, a gradual modification of the epithelium as it approached the hair bulb would become apparent. Near the periphery of the zone represented by the lining of the original follicle, a subdivision of the stratum germinativum into layers representing the outer (deep) and inner (superficial) hair sheaths could be noticed. Somewhat nearer the follicle, the latter would in turn be found to subdivide into a deeper layer of Henle and a more superficial layer of Huxley. Most superficial of all, in a restricted region immediately around the hair bulb, would be a zone of cornified cuticular scales which would now point in the same direction as those on the hair, with which they would form a continuous series. Pushing this comparison still further, the cortex of the hair shaft would seem to correspond to the upper part of the stratum germinativum and possibly the inner hair sheath, while the medulla would represent the lower part of the stratum germinativum, corresponding perhaps to cells of the outer hair sheath. "Prickle-cells like those in unmodified epithelium are found in the medulla of the hair." Such homologies for the parts of the follicle and its contained hair cannot be accepted at present without reservations, especially since there is a good deal of evidence that the inner sheath really grows up from the region of the bulb; but if subsequently established, they may prove of practical significance.

The dermal sheath of the follicle consists of an outer layer of connective tissue fibers arranged longitudinally, an inner layer of circular fibers, and a basement membrane on which the epithelial cells of the outer hair sheath rest, or from which they are separated only by a hyaline membrane of their own production.

The correspondence between the connective tissue around the hair follicle and that beneath the unmodified epithelium is fairly close. The outer layer may be compared to the stratum reticulare and the inner layer to the stratum papillare, except that around the hair follicle no papillae are found.

APPENDAGES OF THE HAIR FOLLICLE

Closely associated with the hair is a sebaceous gland which develops from the same epithelial rudiment and empties into the follicle near the surface, its oily secretion often filling the depression around the root of the hair and ascending by capillarity along the shaft. While a few sebaceous glands occur in places where there are no hairs, as on the margin of the lip, there can be little doubt that there is an intimate developmental and functional relation between the two structures. The true sweat glands have also been thought to have an intimate relation to hair. This idea is based on both morphologic and embryologic

grounds. Jerina quotes Romer to the effect that each hair group has only a single sweat gland. The same view is shared by several others who have been led to the opinion by topographical relations found particularly among monotremes. Diem has shown that in many cases sweat glands develop as outgrowths of the hair follicles. Whatever the relations between hair and sweat glands may be from a phylogenetic and embryologic point of view, there is evidence that they have a certain amount of functional correlation.

One other characteristic structure in connection with most hairs is the arrector pili muscle. This consists of a few smooth fibers that arise in the corium and are inserted on the under side of the hair follicle below the sebaceous gland. Thus located, their contraction pulls the follicle into a more vertical position and causes the hair to stand on end. These little muscles are under the control of the sympathetic nervous system. In some places, they are lacking.

CLASSIFICATION OF HAIRS

The foregoing paragraphs are intended to present a generalized picture of the anatomy and relations of the ordinary type of hair. There are many deviations from this form associated with specialization in various directions. Unfortunately, no wholly satisfactory classification of hairs has been proposed. This is, no doubt, largely due to the complete series of intergrades that can be found between any two hairs, however different they may appear when compared with each other. The following rough tabulation is included in order to afford a general survey of the varied characteristics of hair.

TYPES OF MAMMALIAN HAIR

1. Hairs with specialized follicles containing erectile tissue. Large, stiff hairs that are preeminently sensory. They have been variously designated as, feelers, whiskers, sensory hairs, sinus hairs, tactile hairs, vibrissae, etc. They occur in all mammals except man, and are grouped by Botezat essentially as follows:
   - (1) Active tactile hairs—under voluntary control.
   - (2) Passive tactile hairs—not under voluntary control.
     - (*a*) Follicles characterized by a circular sinus.
     - (*b*) Follicles without a circular sinus.
2. Hairs with follicles not containing erectile tissue. The remaining types of hair, most of which are more or less defensive or protective in function. In many cases, the follicles have a good nerve supply endowing the hair with a passive sensory function as well. These hairs are grouped here according to their size and rigidity.
   - (1) Coarser, more or less stiffened "overhair."
     - (*a*) Spines. Greatly enlarged and often modified defensive hairs, quills.

(*b*) Bristles. Firm, usually subulate, deeply pigmented and generally scattered hairs. "Transitional hairs" (Botezat), "Leithaare" (Toldt), "protective hair," "overhair." This group also includes mane hairs.

(*c*) Awns. Hairs with a firm, generally mucronate tip but weaker and softer near the base. "Grannenhaare" (Toldt), "overhair," "protective hair."

(2) Fine uniformly soft "underhair."

(*a*) Wool. Long, soft, usually curly hair.

(*b*) Fur. Thick, fine, relatively short hair—"under hair," "wool hair."

(*c*) Down. Finest and shortest of hair—"wool," "fuzz."

The tactile hairs that occur in any individual animal are few in number and their distribution is limited for the most part to lips, cheeks and supra-orbital regions. Less commonly they occur on the elbows and knees and even on the back, sides and flanks. Ontogenetically, they are the first hairs to appear and are often the largest hairs of the body. They have deep-seated as well as specialized follicles. Some of them, such as those on the upper lip of the cat, establish connections with the subjacent striated musculature and come under voluntary control. Others are nonmotile. Hairs in the same region of different species of animals may be motile in one case, in the other, not.

The follicle of a tactile hair is shown in Figure 22. The outstanding characteristic of such a follicle is the presence of numerous small or somewhat enlarged blood sinuses in the inner layer of the connective tissue sheath and outside the hyaline membrane. These sinuses, with their walls and interstitial substance, form a little mass of true erectile tissue surrounding the root of the hair and designated as the corpus cavernosum or corpus spongiosum pili. A large individual sinus in the upper part of the body of the corpus spongiosum and encircling the hair root occurs in some forms. This is the "circular sinus." By increasing the turgescence of the follicle, not only is the hair itself made a more efficient conductor of pressure from light contacts, but the nerve endings are also placed in a more favorable position to pick up these impulses. The corpora spongiosa are presumably entirely under the control of the sympathetic nervous system. There is, in addition, a rich sensory nerve supply to the follicle itself, especially to its inner layer, where there are medullated fibers which are said to terminate in small end-organs called Merkel's corpuscles, and nonmedullated fibers which have free terminations (Fig. 23). These structural and functional characteristics make the tactile hairs sense organs of great delicacy, although their importance to the well-being of their possessor has often been greatly exaggerated.

The classes of hairs designated in the table as spines, bristles and awns represent a series with progressively lesser rigidity. The former, as exemplified by those of the porcupine and spiny anteater, are clearly special hairs of considerable defensive value to their possessors. There is no indication that the spines which occur in different mammalian families have any close genetic relation to each other but rather is it more probable, as Gegenbauer has said, that in these cases we see

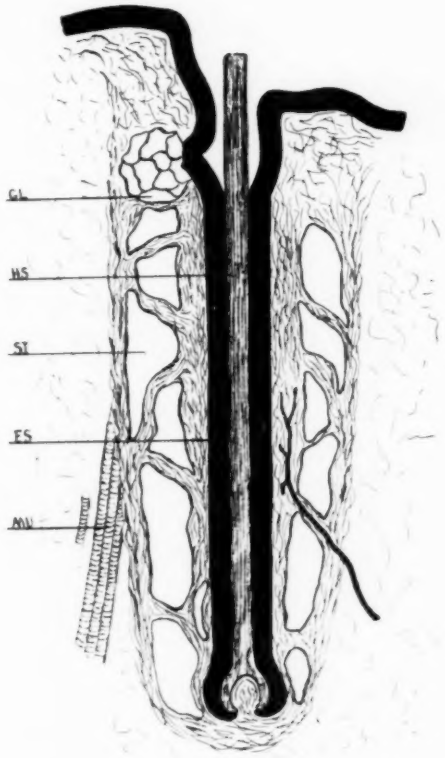

Fig. 22.—Diagram of a tactile hair showing blood spaces in the corpus cavernosum. *GL*, sebaceous gland; *HS*, hair shaft; *SI*, blood sinus, in the corpus cavernosum; *ES*, epithelial sheath; *MU*, striated muscle (characteristic of tactile hairs under voluntary control).

instances of parallelism or convergence, spines having arisen independently in several different lines.

When we come to the bristles, some difficulty is experienced in assigning to them any definite function. They are the long, rather stiff and slender pointed hairs generally sparsely scattered through the pellage. These are the hairs which, in view of their size, usual large number, flattened, imbricate scales and well developed, continuous

medullas, most closely approach the true tactile hairs, from which they differ in the complete lack of a corpus spongiosum. The nerve supply to the follicle is well developed but less elaborate than that of the true tactile hairs. Botezat designates this class as "transitional hairs," and expresses the opinion that they represent the primordial mammalian hair

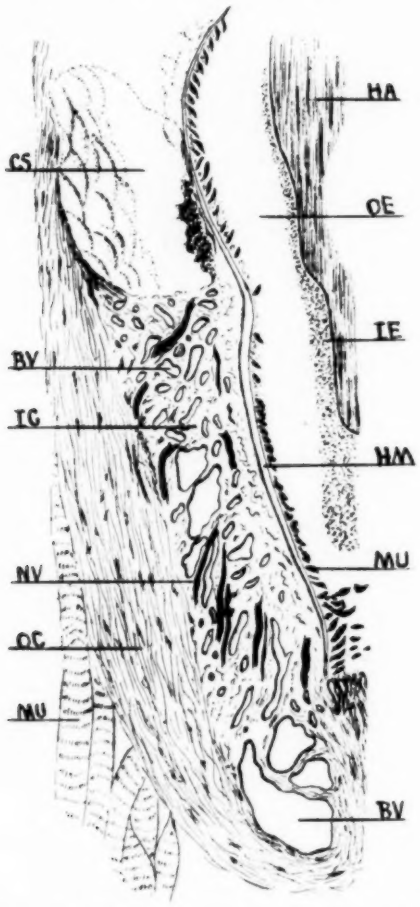

Fig. 23.—Part of the follicle of a tactile hair in the cat (Botezat). *CS*, circular sinus more or less flaccid with the wall to the left thrown into folds; *BV*, blood vessels in the corpus spongiosum or inner connective tissue sheath; *IC*, inner connective tissue sheath (corpus cavernosum); *NV*, nerve fiber; *OC*, outer connective tissue sheath; *MU*, voluntary muscle fibers inserted in the outer sheath; *HA*, hair shaft; *OE*, outer epithelial sheath; *IE*, inner epithelial sheath; *HM*, hyaline membrane; *MU*, a tactile meniscus (Merkel's corpuscle).

type which has given rise in one direction to the several forms of tactile hairs and in the other direction to the more purely protective hairs. Toldt, who finds that in many mammalian pelts there are repeated small

areas, "hair districts" (not the "hair districts" of Pinkus) in which there is one bristle and many progressively smaller hairs (Fig. 24), regards the bristle (Leithaar) as the principle hair in the sense of de Meijere. In commercially prepared fur, these hairs are pulled out or cut off.

The awns are considerably more numerous than the bristles, there being, from Toldt's point of view, several of them to each "hair district." They are characterized for the most part by a firm, dilated and often somewhat flattened tip borne on the end of a less rigid and otherwise furlike hair shaft. Toldt is able to find among the awns of a relatively restricted area every grade of transition, from typical fur to well developed bristles. Like the latter, they have a definite nerve supply.

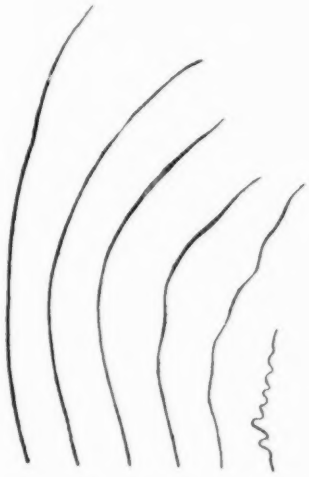

Fig. 24.—Series of finely graded transitions in hairs from the fox, Vulpes vulpes (Toldt).

According to Botezat, medullated nerve fibers enter the connective tissue sheath in the region of the neck of the follicles of smaller awns and both the neck and lower part of the follicles of larger ones.

The remaining three types of hair continue the series of progressively reduced forms. So far as is known, they have no direct nerve supply. The first two may be regarded as purely protective in function, the last as for the most part rudimentary. Wool might properly be designated as a form of fur. Fur hairs are generally fine, soft and abundant. Their scales tend to be relatively large and the medullas more or less reduced or even absent. Ontogenetically, fur and down are the latest hairs to appear. Whether or not they continue to be developed de novo in adult life does not seem to have been determined with absolute certainty, but most evidence is against the idea that they do.

It is doubtful whether anything like a true morphologic entity can be assigned to the several types of hairs. The tactile hairs represent a relatively distinct group, but the other forms are less clearly differentiated. It would be of both theoretic and practical interest to know whether a follicle which would normally produce a fur hair could be made to produce a typical awn or bristle, but direct evidence on this point does not seem to be available. Changes in the character of hairs with age, transitional forms, and hairs that, like some awns, represent essentially different types at the two ends, suggest the possibility that follicles may not be wholly specific in regard to the type of hair they produce. If they are not, an interesting question arises as to why one finds different types of hair growing side by side. In this connection, a more thorough study than has heretofore been made of Toldt's "hair district," if it actually exists, is much to be desired.

The amount, the relative proportions of different types, and the pigmentation of hair show wide variations among the different species of mammals. The number of hairs depends on two different conditions: the extent of hair-bearing skin and the thickness of hair in a unit area of skin.

FACTORS INFLUENCING THE AMOUNT OF HAIR

In most mammals, the amount of skin that is really without hair is very small, but in some the hairless areas are greatly extended. The maximum reduction is found among the whales and dolphins, where the total number of hairs in *Phocaena,* for example, may be as few as two pairs, or in some individuals only one pair of probably useless tactile hairs situated near the mouth. Among other mammals with greatly reduced hair, *Sirenia* is a close rival of the whale. Many thick-skinned animals, such as the hippopotamus, rhinoceros and elephant have lost most of their hair. It is noticeable that the species that have little hair either inhabit warm regions or are supplied with a thick layer of subcutaneous fat, and that such hairs as persist are generally bristles and not fur or down. It has often been assumed that a warm climate is sufficient to cause a direct reduction in the amount of hair, and conversely that cold stimulates hair production. While such views have a certain inherent plausibility, careful scientific data in support of them are far from adequate. In this connection, one must not lose sight of the fact that animals that are not protected against cold can live only in a warm climate, and that some form of protection is requisite for a life in cold regions. There is a wide difference between adaptation through selection and direct physiologic adaptation. That the latter may occur is possibly indicated by seasonal differences in the pelts of some animals. For example, the wild boar is said to have only bristles in the summer, but both bristles and wool in the winter. There are many, for the most

part poorly authenticated, records of change of hair with change of climate. It is claimed that swine at higher altitudes become woolly, and hairless Mexican dogs are said to grow hair after five years in London. Some recent studies of Sumner on the response of mice to continued cold may lead the way to a more accurate knowledge of the immedate and remote effects of temperature on growth of hair.

Knowledge of the relation of increased fat to decreased pilosity also rests on an unstable basis. It has been suggested by those who believe that there is such a relation and think that it has a functional foundation that (*a*) fat under the skin compressed the follicles, causing the hair to atrophy through pressure; (*b*) that the fat absorbs the nutriment, thereby in a sense starving the hair out, which would explain the early disappearance of fine hairs with short follicles, or (*c*) that the fat exercises an unfavorable effect on the sweat and sebaceous glands, thus indirectly affecting the hair. While it is not impossible that some of these factors do affect the amount of hair, it is not easy to find any convincing evidence pointing in that direction. The difficulties in the way of establishing a relation between subcutaneous fat and hair are about the same that are encountered in attempting to establish a similar relation between temperature and hair. In either case, the first desideratum is to determine whether any relation that may exist represents a direct causal connection or is in the nature of a circumstantial correlation. Most writers on this phase of the subject have seemed to imply a belief that modifications acquired by an animal on entering a new environment are transmitted directly to its offspring. This is as yet an unproved assumption.

Closely related to the amount of hair is the relative proportion of the different kinds of hair. There seems to be a widespread phylogenetic tendency among mammals for the finer grades of hair, particularly fur and wool, to disappear or become reduced to down. For bristles, this tendency is much less pronounced. Consequently, as a general thing the more sparse the hairiness, the higher is the proportion of bristles to awns and fur hairs. In many mammals, including the higher apes, the hairy covering consists largely of hairs of the general character of elongated softened bristles. The prevailing reduction of fur in the covering of animals not exposed to very much cold is a familiar phenomenon.

HAIR COLOR

The pigmentation of hair has always been a matter of interest. There are many points in connection with coloration that have not yet been cleared up, but considerable information has been acquired relatively recently through genetic and combined genetic and chemical experimentation. The view sometimes maintained that granular pig-

ment is in reality formed in the connective tissue and subsequently transferred to the hair, has been pretty well disproved by microscopic studies. The theory that individual animal hairs change color has also failed to receive adequate support, changes in the color of pelt having been shown to be due in reality to recurring molts. There seems to be little doubt now that the pigment granules are produced in situ by the cells of the hair bulb itself and undergo little subsequent change. This is probably also true of the soluble pigment. So the coloration of a hair may be considered as in all probability the result of factors acting on hair-forming epithelial elements. The investigation of these factors has yielded some interesting results.

It has been shown that in many of the domestic and laboratory animals, certain grades of color are dependent on the number of pigment granules rather than on their intensity. Specific hereditary "dilution factors" have been found to reduce the pigment granules quantitatively without affecting them qualitatively. When these factors operate in conjunction with those which would otherwise produce black hair, the color becomes slate or maltese. The "dilution factors," which generally behave in heredity as recessives, may be transferred by appropriate crosses to animals of different colors, giving corresponding light or dilute shades. Dilution factors undoubtedly affect soluble pigments as well as the granular form, but here the exact mode of their action is less evident.

Apart from apparent differences in color due to varying amounts and arrangement of pigment, there are also qualitative differences in the pigment itself. Probably all colors due to granular pigment can be resolved into shades of brown, "black" for example being in reality a very dark brown. On this basis, it has been maintained that the different hair colors represent stages in the oxidation of a single pigment base, the color of a hair indicating the stage of oxidation reached in that particular instance. If this is the case, it follows from the variety of definite colors which exist that there is a considerable number of heritable factors which regulate the precise amount of oxidation that shall take place for each hair color. Most of the evidence seems to point in this direction, but the possibility still exists that a single animal species may produce several slightly different melanin bases.

Besides the hair pigments, it has been found that there are two types of whiteness, the dominant and the recessive, or albinotic. The latter is apparently due to the inhibition of a single heritable factor, since it is easily demonstrable by breeding experiments with rabbits or mice that the albinos correspond to all the known color classes except that they are unable to actually develop the color which they have in potential form.

Albinos seems always to carry the color factors unchanged. It is not quite certain whether or not white hair actually contains granules of the unoxidized chromogen base.

The dominant form of whiteness generally associated with spotting behaves in heredity as the exact opposite of recessive whiteness, since a pair of animals with this trait may produce not only offspring like themselves but pigmented young as well. Chemical study of the skins of young rabbits at the time when hair is beginning active growth shows, according to Onslow, the presence of an antityrosinase that prevents the oxidation of tryrosin, which is believed to be one of the important chromogen bases. A few drops of the extract from skin with white hair of the dominant type suffices to prevent the oxidation of extracts from dark skins. In control tests, when the extracts were not mixed, the oxidation of the dark skin was complete.

Various factors which affect the amount and distribution of hair pigment may act at different times on one and the same hair, giving the well-known banded, ticked, or agouti appearance common to many wild animals. This hair pattern is due to another hereditary factor which may be combined at will with the several intensities of black and brown, giving a considerable variety of color effects.

The whole question of pigmentation of animal hair is one that has received a great deal of attention, and relating to which there is a considerable volume of literature. This abridged reference to the subject is made in order to suggest how great is the number of independently hereditary factors that may enter into a relatively simple phase of hair development. It is not meant to suggest, however, that the production of hair pigment involves a complicated reaction. The contrary is probably true. But the process may be controlled, modified or restricted by a surprisingly large number of factors which studies in genetics have shown to exist and which chemical analyses have begun to identify.

There are many obvious lacunae in our knowledge of mammalian hair, but most of the deficiencies are those which we find in other fields of biologic endeavor; they inhere largely in our inability as yet to recognize, analyze and evaluate the determining factors in organ development and maintenance. Whatever is lacking to a comprehensive knowledge of the sequence of developmental stages and structural characteristics of mammalian hair can be supplied with relative ease, but the knowledge of the factors which control these manifestations can at best only keep pace with the advance of an understanding of vital processes in general.

(To be continued)

RAT-BITE DERMATITIS

WITH A REPORT OF A CASE *

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Rat-bite dermatitis is one of the new diseases—not new to the world, for doubtless rats have been biting mankind for milleniums and communicating this disease to human beings, but it is new to medical science. Only within a comparatively few years has it been isolated as a definite syndrome and its etiology determined. And still more recently has it attracted attention in America,[1] and within the past year the first case has come under my observation in Syria. It seems, therefore, of sufficient interest, not to say importance, to put on record.

ETIOLOGY

The etiology of the disease long escaped recognition, for much the same reason that our honored predecessors over four centuries ago for a long time did not connect the eruption, the fever and other manifestations of syphilis with the primary lesion, and were slow to recognize syphilis as a venereal disease. We must be more patient with them than I fear we have been, for with our modern accumulation of knowledge and methods and microscopes and stains and rabbits and guinea-pigs and culture mediums, we have been even slower with rat-bite dermatitis. Moreover, there has been a curious disagreement among investigators as to the infecting germ; some maintaining that it was a diplococcus, others a spirillum, still others a streptothrix. But the honor of demonstrating that the causal agent is a spirochete, *Spirochaeta morsus-muris,* belongs to Dr. Hata of Japan. He was the assistant to the great Ehrlich in his researches for an arsenical cure for syphilis that would be better than mercury; and Dr. Hata is the one who, when Ehrlich felt he was near the end of his list of arsenicals, suggested that he try what was later named arsphenamin. On Hata's return to Japan, his attention was directed to rat-bite dermatitis and its resemblance in so so many features to syphilis on the one hand and to relapsing fever on the other, both diseases caused by spirochetes. He believed that rat-bite dermatitis was also caused by a spirochete. He persevered until he found the spirochete and proved it to be the cause of the malady. This

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* Read before The University Medical Society, Jan. 28, 1924.

1. Meara, F. S.: Treatment of Infectious Diseases, New York, The Macmillan Company, p. 744.

spirochete stains with Giemsa's stain, with Loeffler's methylene blue and with gentian violet, but the best stain, according to Dr. Bellema, my colleague and laboratory assistant, is the Fontana-Trebaudeau stain.

THE BITE OF THE RAT

The bite of every rat does not cause the disease. All rats do not harbor the spirochete in their mouths, and even those infected may not communicate the disease in biting, especially when the rodent bites through clothing, thus brushing his teeth before they enter the skin; and in other cases profuse bleeding from the wound may wash away all entering germs. Recent statistics from Japan report forty-one cases of "Sodoku," as it is called in Japan, where it is said to be better known and has been more intensively studied than in any other country, partly, perhaps, because the light manner of building the houses allows easier access to rats. The disease is now being more frequently reported in America and is attracting considerable attention, enough to warrant Meara to include a chapter on its treatment in his recent work on "Treatment of Infectious Diseases."

INCUBATION PERIOD

The incubation period is said by Arkin [2] to vary from five to twelve days, although some observers put it at from six to eight weeks, or even longer. In some severe cases, in neglected cases and in those already debilitated from other causes, the disease progresses through a long and exhausting course to a fatal termination, even after repeated specific treatment, says Meara.[3]

SALIENT FEATURES

The salient features of the disease are the rat bite, which usually heals quickly, but, after the incubation period, it breaks down and becomes a sclerosis resembling a syphilitic chancre. A spotted erythematous eruption with a coloring and distribution much like the "roseola" of syphilis, pain and aches in the joints and long bones, the headache of syphilis, dizziness and occasional delirium like relapsing fever, a moderate degree of fever as in syphilis, or sometimes a rise to as high as 40 or 41 degrees, and after from three to five days relapse with profuse sweating like relapsing fever of Obermeier; anemia with high leukocytosis, anorexia, nausea and even vomiting, followed by great prostration and in some severe cases ending fatally—these are the broad lines of the clinical picture.

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2. Arkin, cited by Meara (Footnote 1), p. 744.
3. Meara: Treatment of Infectious Diseases, p. 748.

REPORT OF A CASE

History.—On July 7, 1923, my colleague, Dr. Mustafa Khalidy, sent to the dermatology polyclinic, Kaireeyeh Husrum, an unmarried young woman, aged 26. Her family history was irrelevant, as was her previous personal history, which can be given, however, in a few words. She had had malaria, and, in 1919, she had suffered from an attack of bronchial influenza.

History.—On June 10, she was bitten by a rat on the back of the right hand, low down between the metacarpal bone of the thumb and that of the index finger. The wound healed spontaneously in two days, leaving a small scar. But, on or about June 26, she felt severe pain at the site of the bite and noticed considerable swelling; the area was reddish purple and angry looking. It was opened by Dr. Khalidy, but no pus was found. Eight days later, the wound had turned into an angry ulcer, painful, with elevated edges and some sclerosis, with the pain streaking up the arm.

On the skin of the arms, chest and face, and to a less extent on the back and abdomen, were scattered round erythematous blotches about the size of a silver franc piece, which were a bright, light red.

Rat-bite dermatitis was diagnosed, and she was advised to enter the University Hospital for treatment and study. She wished to consult her family first, and did not enter the wards until July 11. Her condition was much the same as when she first presented herself, although there was an extension of the eruption and an accentuation of the color and the intensity of the lesions.

Physical Examination.—The temperature was 38 C., the pulse rate 90, and the respiration 22. The station, gait and reflexes were normal. There was no dizziness, as reported in some cases. The tongue was coated, the appetite poor, and during her stay in the hospital her sleep was poor and broken. The oval ulcer on the hand was 2.5 cm. in its longer diameter, fairly deep and angry looking, with raised indurated edges, not unlike an infected syphilitic sclerosis. The axillary glands on the affected side were palpable and decidedly tender to the touch, although not especially enlarged. Elsewhere, no glandular enlargement could be perceived. Examination of the heart and lungs by auscultation gave negative results. In the first twenty-four hours, she voided 680 c.c. of normally acid, clear, amber colored urine of a specific gravity of 1.015. It contained neither sugar nor albumin. The gravity was low, considering that it was summer and she had fever.

Examination of the sputum showed no tubercle bacilli, but many diplococci and staphylococci and a few streptococci. After the preliminary purge, *Ascarides lumbricoides* were found in the stools. She was anemic, and the blood contained 3,100,000 red cells and 8,000 white cells with 79 per cent. polymorphonuclears, 21 per cent. lymphocytes, 11 per cent. eosinophils and 2 per cent. transitionals. The hemoglobin index was 65. No spirochetes were found in the blood, nor could any be found in the scrapings of the ulcer. This is explained by the fact that there had been an antiseptic dressing on the ulcer for several days.

Treatment.—Despite the negative result of the search for the spirochetes, the diagnosis of rat-bite dermatitis was maintained, and, on July 15, an intravenous injection of 0.45 of neo-arsphenamin was given, and the same applied to the ulcer. Her temperature at 9 o'clock of the morning of the injection was 38.2 C., (100.7 F.), at 2 o'clock it was 38.5 C. (101.3 F.), and at 4 o'clock it reached 39 C. (102.2 F.), from which point it steadily declined to

normal the next day. Her pulse rose with the temperature to 120 beats per minute, but she complained of no especial discomfort. During the afternoon of the day of the injection, the spots increased in number and in brightness, but the next day, they were fading rapidly, and the patient felt so much better that she could not be induced to remain in the hospital, despite the warning that the spots would return if she did not take further treatment.

Three days later, the patient came to the polyclinic with the lesions scarcely visible, and reported that she was feeling fine. She certainly looked remarkably better, her temperature was normal, and she seemed cured, and protested that she was cured. However, ten days later the rose spots reappeared, although they were not as bright nor as numerous as before. A second injection of 0.45 c.c. of neo-arsphenamin was given at the polyclinic, which seemingly eradicated the spirochetes, for she has been free from symptoms of the disease from that time to the date of writing, a period of more than six months. Some authorities advise a series of four or five injections of neo-arsphenamin at intervals of four or five days. In this case, two injections proved enough.

The wound of the bite healed with astonishing rapidity after the first injection, and there was only a slight scar when she came for her second dose.

It is a matter of deep regret that the bacteriology laboratory at the time was closed and that no guinea-pigs were available into which to inject blood from the patient for control.

CONCLUSION

The case is interesting from several points of view.

1. It is a relatively new disease to the medical profession.

2. It is rare—the latest statistics available report forty-one cases in Japan, where it has been studied more than in any other country.

3. It is the first case to be reported in Syria and the only one in the writer's list of more than 70,000 cases of diseases of the skin observed in Syria.

4. The ulcer that breaks down from the bite has an incubation period similar to that of a syphilitic sclerosis. Its general appearance also closely resembles the primary lesion.

5. Many of the general symptoms, notably the eruption and pains, resemble syphilis in the second stage, and in other cases they present strong resemblances to relapsing fever.

6. The case under discussion yielded in our experience with astonishing promptness to neo-arsphenamin. It exemplified "Cito, tute et jucunde!"

THE EFFECT OF GLUCOSE ON THE STABILIZATION OF SOLUTIONS OF ARSPHENAMIN AND NEO-ARSPHENAMIN *

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We have attempted in this experiment to determine the extent to which the addition of glucose to solutions of arsphenamin and neo-arsphenamin would retard oxidation of the solution, and thus prevent deterioration on standing. Glucose has a distinctly reducing action, and it and other sugars have been employed abroad to stabilize solutions prepared in ampules so that the drug could be dispensed in this form without undergoing degeneration or change. The results indicated below are to be interpreted strictly in accordance with the conditions of the experiment, and do not apply to solutions which are kept in a vacuum in sealed ampules. A later publication will deal with this subject.

There is reason to believe that arsphenamin is therapeutically more active than neo-arsphenamin, dose for dose. Nevertheless, the ease of employment of neo-arsphenamin and the better manner in which it is ordinarily tolerated by patients, have led to its more general adoption by the medical profession here and abroad.

It happens, at times, that in administering arsphenamin it is convenient to carry the solution to the home of the patient, or to make it up for some hours in advance of its use. The experiment detailed below has a bearing on the toxicity of solutions which have been kept standing for varying periods of time.

It will be seen from the subjoined tables that an alkalinized solution of a certain lot of arsphenamin was tolerated in 191 mg. per kilogram of body weight. In a solution of glucose, it was tolerated in 200 mg. At the end of twenty-four hours in aqueous solution, the toxicity was increased so that it was tolerated only in 120 mg. per kilogram, whereas in a 5 per cent. solution of glucose, although it had turned brownish, it was still tolerated in 200 mg. per kilogram. At the end of seventy-two hours in aqueous solution, it was tolerated in 100 mg. per kilogram, whereas in glucose solution it was tolerated in 160 mg. per kilogram. All of these animals lived for seven days, the period prescribed for such tests by the United States Public Health Laboratories.

* From the Research Institute of Cutaneous Medicine.

TABLE 1.—*Influence of Standing on Toxicity of Arsphenamin Dissolved in Water and Glucose Solution* *

Arsphenamin Dissolved in Water															Arsphenamin Dissolved in Glucose Solution														
							Results															Results							
				Dose per Kilogram of Body Weight in Mg.	Amount, Hundredths C.c.	Time in Seconds	Days												Dose per Kilogram of Body Weight in Mg.	Amount, Hundredths C.c.	Time in Seconds	Days							
No.	Weight	Sex	Injected at Following Intervals				At Once	1	2	3	4	5	6	7	No.	Weight	Sex	Injected at Following Intervals				At Once	1	2	3	4	5	6	7
1	115	M	At once	120	69	81	—	—	—	—	—	—	—	—	5	120	M	At once	120	72	86	—	—	—	—	—	—	—	—
2	130	M		140	91	109	—	—	—	—	—	—	—	—	6	115	M		140	81	97	—	—	—	—	—	—	—	—
3	120	M		160	96	115	—	—	—	—	—	—	—	—	7	115	M		160	92	110	—	—	—	—	—	—	—	—
4	120	M		191	115	135	—	—	—	—	—	—	—	—	8	115	M		200	115	135	—	—	—	—	—	—	—	—
9	90	M	24 hours, greenish brown	100	45	56	—	—	—	—	—	—	—	—	13	120	M	24 hours, brownish color	120	72	86	—	—	—	—	—	—	—	—
10	110	M		120	66	80	—	—	—	—	—	—	—	—	14	105	M		140	74	88	—	—	—	—	—	—	—	—
11	100	M		140	70	84	—	—	—	—	—	D			15	90	M		160	72	86	—	—	—	—	—	—	—	—
12	110	M		180	99	119	D								16	90	M		200	90	108	—	—	—	—	—	—	—	—
21	110	F	72 hours, precipitated: few drops of alkali added to clear	50	28	34	—	—	—	—	—	—	—	—	21	105	F	72 hours, slightly darker, no precipitates	120	63	75	—	—	—	—	—	—	—	—
22	110	F		100	55	66	—	—	—	—	—	—	—	—	22	100	F		140	70	84	—	—	—	—	—	—	—	—
23	105	F		120	65	78	—	D							23	110	F		160	88	106	—	—	—	—	—	—	—	—
24	105	F		140	74	89	—	D							24	110	F		200	110	133	—	D						

* Test animals; white rats which received intravenous injections.

TABLE 2.—*Influence of Standing on Toxicity of Neo-Arsphenamin Dissolved in water and 5 Per Cent. Glucose Solution* *

Neo-arsphenamin Dissolved in Water															Neo-arsphenamin Dissolved in 5% Glucose														
				Dose per Kilogram of Body Weight in Mg.	Amount, Hundredths C.c.	Time in Seconds	Results																							
							At Once	Days																						
No.	Weight	Sex	Injected at Following Intervals					1	2	3	4	5	6	7	No.	Weight	Sex	Injected at Following Intervals					1	2	3	4	5	6	7
1	100	M	At once	250	63	75	—	—	—	—	—	—	—	—	1	85	F	At once	250	53	64	—	—	—	—	—	—	—	—
2	100	M		300	75	90	—	—	—	—	—	—	—	—	2	75	F		300	56	67	—	—	—	—	—	—	—	—
3	100	M		350	88	103	—	—	—	—	—	—	—	—	3	80	F		350	70	84	—	—	—	—	—	—	—	—
4	100	M		400	100	120	—	—	—	—	—	—	—	—	4	75	F		400	75	90	—	—	—	—	—	—	—	—
5	100	M	1 hour, no change in color	250	63	75	—	—	—	—	—	—	—	—	5	85	F	1 hour, no change in color	250	53	64	—	—	—	—	—	—	—	—
6	110	M		300	83	99	—	—	—	—	—	—	—	—	6	85	F		300	64	77	—	—	—	—	—	—	—	—
7	90	M		350	81	97	—	—	—	—	—	—	—	—	7	90	F		350	79	95	—	—	—	—	—	—	—	—
8	105	M		400	105	126	—	—	—	—	—	—	—	—	8	90	F		400	90	108	—	—	—	—	—	—	—	—
9	110	M	2 hours	250	69	83	—	—	—	—	—	—	—	—	9	75	F	2 hours, no change in color	250	47	57	—	—	—	—	—	—	—	—
10	105	M		300	79	96	—	D							10	95	F		300	71	85	—	D						
11	105	M		350	92	110	—	—	D						11	95	F		350	84	101	—	D						
12	100	M		400	100	120	—	D							12	75	F		400	75	90	—	D						
13	80	M	4 hours, no change in color	100	20	24	—	—	—	—	—	—	—	—	13	80	F	4 hours, no change in color	150	30	36	—	D						
14	100	M		150	38	46	—	—	D						14	90	F		250	56	67	—	D						
15	80	M		250	50	60	D								15	90	F		300	68	82	—	D						
16	75	M		300	56	67	D								16	80	F		350	70	84	D							
17	120	M	24 hours, light brownish green	100	30	36	—	—	—	—	—	—	—	—	17	150	M	24 hours, light brownish green	100	38	46	—	—	—	—	—	—	—	—
18	145	M		200	73	88	—	—	D						18	135	M		200	68	83	—	—	—	D				
19	100	M		250	63	75	D								19	110	M		250	69	83	—	—	D					
20	140	M		300	105	126	D								20	110	M		300	75	90	—	—	D					
21	120	M	72 hours, brownish green	50	15	18	—	—	—	—	—	—	—	—	21	100	M	72 hours, brownish green	50	13	16	—	—	—	—	—	—	—	—
22	115	M		100	29	35	D								22	90	M		100	23	28	D							
23	150	M		200	75	90	D								23	110	M		200	55	66	D							

* Test animals; white rats which received intravenous injections.

The solutions were permitted to stand at room temperature in a 250 c.c. Erlenmyer flask with a cotton stopper. The surface of the solution exposed to the air was approximately 3 inches in diameter.

EFFECT ON SOLUTIONS OF NEO-ARSPHENAMIN

A lot of neo-arsphenamin dissolved in water was tolerated by white rats for a period of seven days in a dose of 400 mg. per kilogram. Dissolved in 5 per cent. glucose solution, it was tolerated in the same dosage. At the end of one hour, no change in color had taken place in either solution, and the drug was tolerated in the same dose of 400 mg. per kilogram. At the end of two hours' standing, the toxicity had been increased, both in the aqueous and in the glucose solution, so that the drug was tolerated only in 250 mg. per kilogram. At the end of four hours, although no change in color had taken place, it was tolerated in each solution in about a dosage of 100 mg. per kilogram. At the end of twenty-four hours, both solutions had become a light brownish green, and the drug was tolerated in 100 mg. per kilogram. At the end of seventy-two hours, both solutions had become brownish green, and the drug was tolerated in each in 50 mg. per kilogram. The foregoing figures indicate that under the conditions of the experiment the addition of glucose to solutions of neo-arsphenamin does not effect a stabilization.

Various attempts have been made in this country and abroad to place on the market solutions of arsphenamin and neo-arsphenamin ready for use. There can be no doubt that solutions of arsphenamin can be prepared so that there is no increase in toxicity, and indeed there may even be some decrease in solutions on long standing under proper conditions. Another important factor, however, must be considered in determining the value of such solutions. If a reduction of toxicity takes place, as is alleged, this means that chemical change has resulted, and such chemical change may conceivably affect the therapeutic power of the drug. A forthcoming communication will deal with this subject.

CONCLUSIONS

1. The addition of 5 per cent. of glucose to solutions of arsphenamin appears to retard oxidation for a period of twenty-four hours under conditions of the experiment described, so that, at the end of this period, the drug is tolerated in the same dosage as when injected at once. At the end of seventy-two hours, there is a 20 per cent. increase in toxicity as compared with the fresh solution.

2. The addition of 5 per cent. of glucose to solutions of neo-arsphenamin, under conditions of the experiment described, does not delay oxidation or lessen toxicity.

3. Deductions from this experiment are only applicable to the particular brand of arsphemanin and neo-arsphenamin employed, as there might conceivably be different results with other brands.

News and Comment

"CONGENITAL ECTODERMAL DEFECT"

To the Editor:—In our article entitled "Congenital Ectodermal Defect" published in THE ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY for December, 1924, an unintentional injustice was done Dr. Henry B. Richardson of the Russell Sage Institute of Pathology. Our patient was investigated by Dr. Richardson in connection with extensive original basal metabolism research with the calorimeter. Through an unfortunate misunderstanding, his tests on our patient were published in our paper without specific permission, and while we credited the Institute with the work we failed to state that the tests were part of the original investigation being conducted by Dr. Richardson.

In an editorial published in *The Journal of the American Medical Association* for Feb. 14, 1925, which comments on our article, the reader gains the impression that we did the basal metabolism work, which, of course, is erroneous.

The misunderstanding has interfered with the publication of Dr. Richardson's work, for which we are very sorry.

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Abstracts from Current Literature

Observations on the Treatment of Primary and Secondary Syphilis. B. A. Thomas, Am. J. Med. Sc. **168**:697 (Nov.) 1924.

This is a general review of the methods in use at present in the treatment of syphilis. Emphasis is placed on the early diagnosis of the disease (in the case of primary lesions) and on the continuation of treatment for at least two years in secondary cases, even though the Wassermann test soon becomes negative.

Two New Antimony Compounds for Intravenous Use. A Study of Their Therapeutic Value in Cases of Granuloma Inguinale. Alexander Randall, Am. J. Med. Sc. **168**:728 (Nov.) 1924.

Sodium antimony thioglycollate (referred to as S. A. T.) and triamide of antimony thioglycollic acid (referred to as T. A. T.), two synthetic compounds, were found to be of lower toxicity than tartar emetic and failed to show any evidence of antimony poisoning and produced no irritation at the site of injection. Nine out of ten cases of granuloma inguinale were promptly cured clinically, with immediate relief from pain in three patients. Further studies are under way regarding the value of these two new drugs in the treatment of syphilis. The ten treated cases are reported in detail.

Syphilitic Aortic Insufficiency. R. W. Scott, Arch. Int. Med. **34**:645, (Nov.) 1924.

A description is given of twenty-five cases of this disease in which all cases presented a syphiltic mesaortitis and hypertrophy with some degree of dilatation of the heart, chiefly of the left ventricle.

Jamieson, Detroit.

Xeroderma Pigmentosum. A Clinical and Pathological Report of One Case. A. R. Rich, W. C. Davison and C. G. Green, Bull. Johns Hopkins Hosp. **35**: (Sept.) 1924.

The authors report a typical case of xeroderma pigmentosum occurring in a patient aged 2 years. Brown freckles first appeared over the face. These gradually became pustular and exuded a purulent discharge. They then became encrusted and resembled hard warts. The individual lesions then gradually increased in size, and many of them coalesced. The condition also involved part of the skin of the neck. Eighteen months after the onset, one of these warts developed on the side of the nose, grew rapidly and finally eroded part of that organ. The hands and arms were also involved. The lesions were pruritic.

1. A biopsy was made of what appeared to be normal skin from the buttock. There were certain cellular changes which suggested a beginning atrophy of the epidermis, with a coincident increase in the amount of melanin pigment within the epithelial cells and corium.

2. A biopsy was made of a smooth, shiny, atrophic looking, lightly pigmented piece of skin from the abdomen. Microscopically, it showed an extreme atrophy and disorganization of the epithelium, with pigmentation; but there was no noticeable change in the vascular, connective or elastic tissue elements of the corium.

3. A biopsy specimen taken from the neck included a small wart-like excrescence and a darkly pigmented portion of otherwise normal appearing skin. Epithelial atrophy, which became extreme, marked pigmentation and beginning proliferation of the epithelium in localized areas to form benign wart-like growths were found.

4. The biopsy specimen from the cheek was a small, slightly elevated bright red area with telangiectasis. The contiguous skin was pale and smooth, and had the appearance of an old scar. This showed, microscopically, a slight epithelial change, but a marked increase in the connective tissue and an almost complete disappearance of elastic fibers of the corium.

5. A biopsy specimen was taken from a small warty excrescence. Microscopically, it showed the development of a wartlike tumor, with slight invasive properties in a portion of the corium.

6. Biopsy of a fungoid warty tumor showed four epithelial tumors of distinctly independent origin, which ranged in size from a very small proliferation of only a few cells, through a large benign wart, to a larger malignant, invasive epithelioma. There were no abnormal deposits of pigment.

7. A small warty nodule was removed from the neck before radium treatment was instituted. This showed a rather invasive epithelioma and a replacement of corium by a fresh growth of connective tissue which appeared to be a true connective tissue tumor.

The authors state that it is usually believed that this disease follows a course which may be divided into four stages: first, the stage of inflammation and reddening of the skin; second, the stage of pigmentation; third, the stage of atrophy, roughening of the skin and telangiectases; and finally, the stage of tumor development. But its progress is not so definite.

Radium exerted no permanent beneficial effect.

The patient died at the age of 4, but no evidence of metastases was found.

McCafferty, New York.

Epinephrin in the Treatment of the Pain of Herpes Zoster. W. W. Duke, J. A. M. A. **83**:1919 (Dec. 13) 1924.

Duke has found that the pain associated with zoster is relieved promptly but only temporarily by epinephrin in about 50 per cent. of the cases. The dose varies with the individual, but the drug should be given until relief is obtained or distinct tremor prevents its further employment for the time being.

Vincent's Angina Occurring in a Patient Under Treatment for Syphilis. I. C. Sutton, J. A. M. A. **83**:1919 (Dec. 13) 1924.

The patient had been given three intramuscular injections of sulpharsphenamin at short intervals when she developed Vincent's infection of the mouth. This infection healed promptly under the local application of an arsphenamin glucose solution.

Sutton reports the case as an instance in which arsphenamin failed to protect against Vincent's infection, and especially because arsphenamin intravenously has been recommended for this disorder.

A Case of Hypersensitiveness to Carbon Tetrachlorid. H. F. Taylor, J. A. M. A. **84**:280 (Jan. 24) 1925.

The author records a vesicobullous dermatitis in himself from external contact with this chemical. In one attack, both the hands and oral mucosa

were affected. He is also sensitive to iodoform, and thinks it is suggestive that both poisons are methane derivatives.

STUDIES IN ADDISON'S DISEASE. L. G. ROWNTREE, J. A. M. A. **84**:327 (Jan. 31) 1925.

Rowntree presents an extensive clinical and laboratory analysis of forty-seven cases. In twelve cases coming under his personal supervision, he has used epinephrin to the point of tolerance, with decidedly good effect, considering the formidable character of the disease. Epinephrin is given by mouth, rectum and hypodermically to the point of tolerance. Five of the patients died under treatment, two patients have been under observation for too short a time to justify deductions, while five are alive and in good condition after periods of observation ranging from thirteen to twenty-six months.

While the administration of epinephrin is only substitution therapy without effect on the cause of the disease, the favorable results obtained in this series justify its use in every case of Addison's disease. Every other measure of possible benefit should be employed coincidently.

ACTION OF ACRIFLAVINE ON THE BLOOD AND CERTAIN TISSUES OF RABBITS, WITH PARTICULAR REFERENCE TO HEMOLYTIC STREPTOCOCCUS SEPTICEMIA. F. L. MELENEY and ZUNG-DAU ZAU, J. A. M. A. **84**:337 (Jan. 31) 1925.

The authors conclude that the bacterial inhibiting action of neutral acriflavine within the body is so slight, even in lethal doses, that it is not a legitimate intravenous medication in hemolytic streptococcus infections.

It has a deleterious effect on the kidney and liver, apparently having a selective activity for these organs.

PHOTOMICROGRAPHIC STUDIES OF MORPHOLOGY OF SURFACE CAPILLARIES IN HEALTH AND DISEASE. 1. THE ANATOMY OF NORMAL SURFACE CAPILLARIES AND A PHOTOGRAPHIC METHOD OF THEIR OBSERVATION AND RECORDING. C. L. CALLANDER, J. A. M. A. **84**:352 (Jan. 31) 1925.

Callander describes an apparatus with which he has been enabled to photograph the papillary capillaries and the subpapillary plexus. His observations of normal capillaries at the root of the nail showed that these vessels vary greatly in form and size. Bizarre shapes are seen. The circulatory flow is readily observed. The venous capillary limb is larger than the arterial and can often be traced deeper.

This introductory report is accompanied by several photographs of normal capillaries.

LIPOMA OF THE SCALP: REPORT OF CASE. G. D. CUTLER, J. A. M. A. **84**:421 (Feb. 7) 1925.

The patient, aged 2 years and 4 months, presented a rather large lipoma of the scalp, which was removed surgically. Lipoma of the scalp is rare, especially in childhood.

PREVENTION OF CONGENITAL SYPHILIS BY TREATING THE MOTHER DURING PREGNANCY. J. S. LAWRENCE, J. A. M. A. **84**:432 (Feb. 7) 1925.

The author has collected the data from a number of municipal clinics in New York State relative to this question. The treatment given approximates

that commonly employed, consisting of arsphenamin and mercury given simultaneously in courses of eight injections of the former and fifteen of the latter.

There were seventy-six complete case records available, eleven primiparous and sixty-six multiparous. The latter had conceived 256 times, with only 114 living children.

Following treatment of eighteen multiparous women with no living children, fourteen had borne a living healthy child. Following treatment, forty-seven multiparas had fifty-four conceptions, eight not terminated. The forty-six remaining conceptions resulted in thirty-eight living infants.

From these results, Lawrence is able to confirm previous reports of the valuable effect of antisyphilitic treatment of the expectant mother.

MICHAEL, Houston, Texas.

CONTRIBUTION TO THE TREATMENT OF CANCER OF THE LIP BY IRRADIATION. B. F. SCHREINER and L. C. KRESS, J. Cancer Res. **8**:221 (July) 1924.

During an eight year period, 136 patients were treated with roentgen-rays at the State Institute for the Study of Malignant Diseases at Buffalo. The lesions treated were clinically diagnosed squamous or prickle-cell epithelioma and were divided into three groups: (1) those with no demonstrable involvement of the lymphatics, (2) those with definite metastatic involvement of the lymph channels but considered surgically operable, (3) those with advanced or "fixed" metastases and considered inoperable. Unfiltered roentgen rays were used, and the primary lesion was given from one to three erythema doses in one treatment, depending on the thickness of the lesion. The lymphatics were not treated in the first group, but in the second group the submental and submaxillary areas were exposed to erythema dosage of rays filtered through 3 mm. of aluminum. Some gland areas were treated with radium packs, but at present high voltage roentgen-ray treatment is the routine.

Group 1 comprised sixty-nine cases, and showed 78 per cent. well over a three year period and 52 per cent. well over a five year period. Group 2, including thirty-six cases, showed 39 per cent. well for 3 years and 30 per cent. well for five years. The thirty-one cases of Group 3 failed to show clinical cures, and it was decided that it was inadvisable to use irradiation in that type of case.

The authors claim that a fair percentage, in their study 34 per cent., of the operable type of lip epithelioma can be healed by roentgen-ray therapy alone. They consider the papillary or proliferating type of primary lesion as more amenable to successful treatment than the infiltrating type, and state that in the latter type the implantation of bare tubes of radium appears to be the proper treatment.

THE RELATION OF RECKLINGHAUSEN'S DISEASE TO GIANT GROWTH AND BLASTOMATOSIS. F. WINESTINE, J. Cancer Res. **8**:409 (Oct.) 1924.

The author reports a case, with detailed necropsy findings, and comments on etiology.

Multiple neurofibromatosis is considered to be due to a congenital anomaly of the ectodermal-mesenchymal components of the nervous system. It is considered as frequently associated with a dysontogenesis of other body tissues.

In this case, there was an associated giant growth and neurofibromatosis of definite sectors of the intestine and mesentery and of their corresponding nerves.

H. R. FOERSTER, Milwaukee.

STUDIES ON THE BIOLOGY OF STREPTOCOCCUS. IV. THE OCCURRENCE OF STREPTOCOCCUS SCARLATINAE IN CONVALESCENCE AND IN THE COMPLICATIONS OF SCARLET FEVER. F. R. STEVENS and A. R. DOCHEZ, J. Exper. Med. **40**:493 (Oct.) 1924.

After isolating by agglutination tests a group of streptococci from 65 per cent. of scarlatinal patients in the first week of the disease, it was found that strains of hemolytic streptococci belonging to this group could be isolated from throats after quarantine. These strains were found most frequently in convalescent patients with incomplete involution of tonsillar inflammation, the complications of scarlatina being due either to the original strain or to secondary infection.

THE PRODUCTION OF PERSISTENT ALOPECIA IN RABBITS BY ROENTGEN RADIATION: A STUDY OF THE MINIMUM DOSE REQUIRED AND THE CONSISTENCY OF THE REACTION. H. CLARK and E. STURM, J. Exper. Med. **40**:517 (Oct.) 1924.

The critical dose necessary for the production of permanent alopecia in rabbits was found to correspond to the production of 2.04×10^{15} ions of either sign per gram of tissue.

THE PRODUCTION OF AN EXOTOXIN BY CERTAIN STRAINS OF STAPHYLOCOCCUS AUREUS. JULIA T. PARKER, J. Exper. Med. **40**:761 (Dec.) 1924.

Through rabbit experimentation with certain strains of *Staphylococcus aureus*, it was found that sterile Berkefeld filtrates of both cultures had a selective poisonous action on the skin, this poison being completely destroyed at 55 C. for one hour, being capable of stimulating antitoxin production when injected intradermally.

JAMIESON, Detroit.

LICHEN SPINULOSUS, AN UNUSUAL TYPE. A. MIBELLI, Gior. ital. d. mal. ven. **59**:1741 (Dec.) 1924.

The unusual case reported by the author was that of a boy, aged 12, who presented numerous small, hyperkeratotic papules, situated on the extensor surfaces of the arms and legs, the dorsum and the back of the hands. Microscopically, the lesions showed inflammation of the sebaceous and sweat glands and hyperkeratosis of the follicles. The author suspects that this condition is due to a peculiar reaction of the skin in cases of latent tuberculosis.

ANNULAR ERYTHEMA CENTRIFUGUM. DARIER. H. DE BELLA, Gior. ital. d. mal. ven. **59**:1757 (Dec.) 1924.

The author reports a case of eight months' duration in a woman who had chronic metritis and rectitis. The condition was probably due to focal infection. The patient improved greatly after treatment for the genital and rectal infections.

SYPHILITIC CHANCRE OF THE SCALP. C. FELUGO, Gior. ital. d. mal. ven. **59**:1850 (Dec.) 1924.

The patient had a large primary lesion, the size of a silver dollar situated on the left side of the frontoparietal region, which he contracted in a barber shop.

ANGIOKERATOMA MIBELLI. UGO TOMASONE, Riforma. med. **40**:1057 (Nov. 10) 1924.

From the study of a personal case, the author concludes that angiokeratoma is due to a pathologic condition of the blood vessels of the skin which become dilated. Hyperkeratosis is secondary to this angiectasis. This vascular condition is brought about by an infectious or toxic agent, the tubercle bacillus in his case. Pathologically, the changes observed in the tissues are not those of tuberculosis. Angiokeratoma may be classified among the "tuberculoides" of Darier.

RAYNAUD'S DISEASE AND WEIR MITCHELL SYNDROME CURED WITH NEO-ARSPHENAMIN. G. MARTINI, Riforma med. **40**:1169 (Dec. 8) 1924.

This is a report of a case of symmetric gangrene and acrodynia of the hands, feet and ears in a boy 15 years old. The patient had stigmas of hereditary syphilis, and the Wassermann test was strongly positive. There was a rapid improvement under treatment with neo-arsphenamin. The patient was permanently relieved.

LEUKOPLAKIA OF THE PREPUCE AND BALANUS. C. MADERNA, Riforma med. **40**:1177 (Dec.) 1924.

This article contains the report of a case of extensive leukoplakia of the mucous membrane of the penis in a man 71 years old. Intramuscular injections of bismuth and local applications of radium cured the condition.

TREATMENT OF CANCER OF THE PENIS. S. BARABINO, Prensa med. Argentina **11**:553 (Nov. 20) 1924.

Treatment by the roentgen-rays and radium in cancer of the penis was not encouraging in five cases reported by the author.

PARDO-CASTELLO, Havana.

CHANGES IN THE BLOOD PICTURE AFTER INJECTION OF ARSPHENAMIN WITH PARTICULAR CONSIDERATION OF COMBINED EPINEPHRIN AND ARSPHENAMIN INJECTION. Y. TAKENCHI, Acta dermat. **4**:74 (Sept.) 1924.

Twenty-five rabbits were divided into two groups. The first group received only one injection, while the second received several injections. Some received the normal dose (0.01 gm. per kilogram) and others maximal doses (0.1 gm. per kilogram). The preparations used were neo-arsphenamin and arsphenamin. According to the author, the injections had no influence on hemoglobin content or on the red blood cells, but the leukocytes were always lessened in number. When epinephrin was given before the injection of neo-arsphenamin, the eosinophils decreased.

SEROLOGIC STUDIES OF EXPERIMENTAL SYPHILIS. S. TAKENAKA, Acta dermat. **4**:75 (Sept.) 1924.

In an excellent study of the Wassermann reaction in normal rabbits, in syphilitic rabbits and in rabbits having a disease (due to *Spirochaeta cuniculi*) closely akin to rabbit syphilis, the author draws the following conclusions:

(1) The so-called nonspecific positive Wassermann reaction in healthy rabbits, though not absolutely absent, appears only occasionally when proper

precaution is taken and is of a degree which does not interfere with the investigation of the Wassermann reactions of the rabbit. In my work, the nonspecific positive reaction constituted about 1 per cent. of the entire groups of the rabbits.

(2) The amount of the serum proper for testing the Wassermann reactions is 0.2 c.c., and the antigen suitable for the purpose is the alcoholic extract of the ox heart treated with ether and again with acetone according to Noguchi's method.

(3) The primary sclerosis of rabbit syphilis and the Wassermann reactions generally progress in close agreement with each other. The infection or non-infection of the testis seems to have a great significance in inducing the positive Wassermann reaction.

(4) The appearance of the general symptoms, such as keratitis, does not give rise to a positive Wassermann reaction.

(5) The effect of reinoculation on the Wassermann reaction depends on whether the primary sclerosis is produced or not.

(6) According to the antigens used, the degree of positive reaction and the percentage of nonspecific reaction differ.

(7) In the diseases producing sclerosis in rabbits resembling that of syphilis — due to *Spirochaeta cuniculi* or the spirochete of rat-bite fever — even when the testes are chiefly attacked, the Wassermann reaction is always negative.

(8) Judging from these results, the Wassermann reaction of rabbit syphilis is considered specific; however, the reactions differ greatly from those in human syphilis in that the Wassermann reaction becomes negative on the disappearance of the primary sclerosis in this animal, and also in that the appearance of the positive reaction depends to some extent on whether the testis is affected or not.

STUDIES IN LYMPH GLANDS: DEMONSTRATION OF LEPRA BACILLI BY PUNCTURE OF LYMPH GLAND. S. MATSUMOTO and S. TAKENAKA, Acta dermat. **4**:115 (Sept.) 1924.

In an examination of more than 150 cases of leprosy, the authors found that a general lymphadenitis leprosa may or may not exist, and therefore a pathognomonic clinical feature in reference to the form or consistency of the lymph nodes does not exist, as in syphilis, for example. "Regional" lymphadenitis is not demonstrable. In puncturing the glands, those in the inguinal or crural regions were found to be the most suitable for operation as better fixation could be obtained. A 1 c.c. syringe containing 0.5 c.c. of physiologic solution of sodium chlorid and fitted with a snugly attached 1/1 mm. needle was used. The salt solution was injected and withdrawn several times from the glands, and the fluid thus obtained spread on slides and stained with the Ziehl-Gabbet method. In seventy-six cases in which puncture was successful, the bacilli (showing a typical arrangement in the form of cigaret-like bundles mingled with isolated organisms and granules) were demonstrated in all cases of lepra tuberosa, in 60 per cent. of lepra maculosa and in 58 per cent. of lepra erythematosa. Thus in approximately two thirds of the lepers the bacterial finding in the lymph gland was positive. These findings show that bacilli are not infrequently seen abundantly in glands of patients having only slight neuritis or maculae.

"Safu," a Symmetrical Vitiliginous Condition in the Inhabitants of Turk Island in the South Seas. T. Matsumoto, Acta dermat. **4**:147 (Oct.) 1924.

The author reports peculiar symmetrical vitiliginous changes on the extremities called safu or tinea intersecta. Although it is proved that this condition is not tinea albigena, further study will be necessary to identify and classify this disease.

The Influence of X-Rays on the Hemolytic Complements. K. Niskiura, Acta dermat. **4**:155 (Oct.) 1924.

Serum of healthy guinea-pigs, which contains normal hemolytic complement, was thinned out to various dilutions and treated with roentgen rays of different dosages. The author came to the following conclusions:

(1) Hemolytic complement is not influenced by small doses of roentgen ray. It is with ten erythema doses or more that any effect is noted.

(2) Two containers containing hemolytic complement and situated 1.5 mm. and 5 mm. from the source of the rays showed no difference in the destruction of the hemolytic complement.

(3) In irradiating hemolytic amboceptor or normal hemolytic complement containing the serum of guinea-pigs, there is produced neither an antihemolysin nor an anticomplement substance.

Contribution to the Clinical Study of Yaws. S. Takesaki, Acta dermat. **4**:165 (Oct.) 1924.

In a detailed clinical study of twelve cases of yaws observed at the Palau Hospital, South Sea Islands, the author points out that when we observe the cases of yaws in detail, we find that the clinical appearances of the disease, as in syphilis, are pleomorphic, presenting nearly all the forms of syphilitic changes. There exist also a number of forms differing more or less from those of syphilis. As features of special interest, the author notes the involvement of bones (of forearm, hand, sternum and ribs) in two cases; in another case, sabre-shaped deformity of the tibia; one case in which there was paronychia as well as lichenoid, psoriasiform and eczematoid eruptions; two cases which showeed an eruption almost similar to lichen syphiliticum or lichen scrofulosorum. The last two cases described showed psoriasiform eruptions on the palmar and the plantar surfaces.

A strict differentiation of yaws of this type from syphilis is difficult, and this is especially true if the cases belong to the tertiary stage. Excellent photographs illustrate the article.

Juxtra-Articular Nodosities of Jeanselme. S. Takasaki, Acta dermat. **4**:229 (Nov.) 1924.

The author studied fourteen cases of this condition encountered in the South Sea Islands. In differential diagnosis, he rules out ordinary fibroma, syphilis, tuberculosis, leprosy, elephantiasis, frambesia and xanthoma, and believes that we are dealing with a peculiar type of inflammatory fibroma whose exact cause is still unknown. Neither parasitic fungi nor spirochetae can be considered to be the causative agent.

ORCHITIS OF THE RABBIT EXPERIMENTALLY PRODUCED BY INOCULATION WITH THE SPIROCHETE OF RAT-BITE FEVER. SATOSHI TAKENAKA, Acta dermat. **4**:271 (Nov.) 1924.

In the course of the studies in experimental syphilis of the rabbit which have been going on for several years, it was found necessary to perform a series of parallel experiments with some other spirochetes resembling *Spirochaeta pallida*. In these studies, the author found that the spirochete of rat-bite fever originated from a human case and transmitted from mouse to mouse in succession through many generations is able constantly to produce orchitis in rabbits following intratesticular inoculation. The process affects the testicle tissue uniformly. The disease can be divided into four stages: first week, incubation; second week, the stage of active progression; third week, the stage of regression; fourth and fifth weeks, edematous swelling of the prepuce and perianal region.

McCARTHY, Washington, D. C.

OBSERVATIONS ON THE SENSE OF PAIN IN SKIN EXPOSED TO ULTRA-VIOLET RAYS. V. MALMSTRÖM, Acta radial. **3**:327 (Aug.) 1924.

This investigator has observed hyperalgesia, following exposure to either sunlight or the rays of the quartz lamp, during the latent period after the heat erythema has subsided and before the light erythema has appeared. He also observed that sensations following contact with sharp or dull objects at such a time were abnormally prolonged, and painful sensations once produced continued and were localized in spite of procain anesthesia at the site sufficient to prevent recording of new impulses. These same sensory reactions were observed after subsidence of ultraviolet light erythemas. When the rays were passed through a quartz vessel containing a 1 per cent. solution of quinin sulphate, which completely absorbs all ultraviolet rays, there were no changes in skin sensation reactions in patients who otherwise reacted in the manner described above. These reactions are attributed to a direct light action on the intra-epithelial nerve endings for pain perception, which reaction is thought to lower the threshold-value of such perception. It is also thought to increase the range of activity of these nerve endings.

An Alrutz algesimeter and a 220-volt quartz burner were employed in the experiments. The exposure time was from four to five minutes, the distance 25 cm. and the volar side of the arm was the area usually exposed.

Twenty-one experiments were carried out and carefully checked and controlled. The physiologic considerations of pain perception were discussed.

H. R. FOERSTER, Milwaukee.

Society Transactions

NEW ENGLAND DERMATOLOGICAL SOCIETY

Quarterly Meeting, Oct. 8, 1924

HENRY J. PERRY, M.D., *Presiding*

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. FAULKNER.

A young Italian, aged 21, had an eruption of two months' duration. He first noticed a large indurated patch of erythema on the abdomen; it did not itch, but was tender to pressure. His physician gave him three intravenous doses of some white substance. The lesions were unimproved. About a week before admission, his throat began to feel sore, and three days before admission the eruption became very much more generalized, coming out on his face in the same kind of indurated erythema, slightly raised. On admission to the hospital, he presented a marked erythema on his body and face, especially on his forehead — raised red areas, a few of which had broken down and become crusted. His throat presented marked ulceration on the right side between the uvula and the palate. He was admitted to the ward the same day. The Wassermann test was negative. Throat cultures showed a few spirochetes, resembling Vincent's, also streptococci. Blood cultures were negative. He developed a number of bullae on his body. These were negative to tests for syphilis. The ulcer of the throat became very much worse, and the entire uvula sloughed away, leaving a punched out area between the tonsils without touching the tonsils at all. He was given two doses of neo-arsphenamin, and neo-arsphenamin was applied locally to the lesions in the throat. After about three weeks in the ward, with a temperature varying from 101 to 103 F. and a gradually rising pulse rate, he was given antierysipelas treatment during the day and a sulpho-ichthyolate ointment at night. Under this treatment, he began to improve, and the temperature gradually subsided, but the condition of the skin remained about the same. The crusts had fallen off some of these areas, leaving atrophic areas. There was a general glandular enlargement. The blood picture was perfectly normal; the temperature at time of presentation was normal. Dr. Faulkner said he was of the opinion that the case was one of lupus erythematosus disseminatus.

DISCUSSION

DR. E. LAWRENCE OLIVER said that the case presented looked to him somewhat like an acute case of mycosis seen at one time in his Department, and that when the first lesion in that case had appeared, Dr. Abner Post had thought that it was a primary lesion. A few weeks later when a general eruption had broken out, it had looked somewhat like a large secondary eruption. The whole course of that case had been but three months, and it had had a fatal issue. The present case, he said, reminded him of that case on account of the red raised tumors. He said he did not see how one could make a diagnosis of lupus as the scaling seen in lupus erythematosus was lacking and the distribution seemed rather extraordinary.

DR. FAULKNER replied that Dr. J. Harper Blaisdell had made the diagnosis, and that it depended largely on the configuration on the face and forehead.

In a study of the literature, they had not been able to find a case with as extensive lesions as this one.

Dr. Arthur M. Greenwood said that he thought it was more like mycosis.

Dr. C. Morton Smith said that he recalled the case Dr. Oliver spoke of and that they had not seemed to reach any conclusion in it. The patient had been treated in the western part of the state for syphilis, and he showed lesions on the face that could have been used for illustration of sarcoid. One could pick out isolated lesions that looked exactly like that condition. The man also had typical rupial lesions over the arms and in some other places. One might have used these lesions in demonstrating a rupial syphilid. Some of the physicians in the room in which diseases of the throat were treated had felt that Vincent's angina was the correct diagnosis.

Dr. C. Guy Lane said that he had seen the present case on the first day the patient appeared, and with the indefinite history obtained, he thought that the condition might be erythema multiforme. After discussing the case with Dr. Blaisdell, he had read what Sutton says in regard to the description of lupus erythematosus disseminatus, and he felt that the case fitted into that class very well. Dr. Lane said that he had not realized before that there were vesicular and bullous lesions, but Sutton speaks of them.

Dr. Faulkner said that a roentgenogram of the chest had been taken and tuberculosis eliminated. He said that the patient was a little weaker than when he came in, but fairly comfortable. A good many of the crusts of the skin lesions had fallen off, leaving atrophic white areas. No new bullae had appeared since the man came to the hospital — only papules. The temperature was irregular, varying from 102 to 99 F.

Gumma of the Sclera. Presented by Dr. Henry D. Lloyd.

A young woman with a growth in the right eye came to the Dispensary about five years before. A diagnosis of tuberculous disease was made, but Dr. Coues did not endorse that. The belief was that the growth was due rather to syphilis. While in the hospital, the condition healed perfectly. The young woman had continued to receive intermittent treatment, with no really visible manifestations since that time. From time to time, she had complained of some indefinite pain in both arms but more marked in the right, usually following practising or playing on the piano. Under external treatment it usually disappeared. She came to the clinic concerning the eye condition about a month before presentation. She was seen by Dr. Smith and Dr. Lloyd, then by Dr. Derby, and there was difference of opinion as to the etiologic factors, Dr. Derby favoring a tuberculous basis for the present process, and Drs. Smith and Lloyd believing that one etiologic factor can explain both. The patient had received two inoculations — one a month before and one the evening before presentation. She had also received as much potassium iodid as she could take, starting, Dr. Lloyd thought, with 15 drops and going up to 30. Dr. Smith and Dr. Lloyd agreed that the process showed slight improvement. Dr. Lloyd said that gumma of the sclera was rare, and that he did not know how the diagnosis could be proved except by biopsy.

DISCUSSION

Dr. Smith said that there was one more factor that they had thought important during the last few days, and that was the color in the central portion of the new growth; the growth had flattened out definitely, so that it was now more of a plaque, whereas the other day it was almost hemi-

spheroidal. The center had a definite yellowish mass underneath the dilated blood vessels, much like the appearance observed in gummatous lesions elsewhere. If it were a case of tuberculosis such changes as had occurred under iodid treatment — even the flattening — could hardly be expected to occur in the same length of time. She had received some mercury. Dr. Smith said that he agreed that gummatous lesions on the sclera were rare.

Dr. William P. Coues said that he had been extremely interested in the case, and that Dr. Lloyd had seen the patient with him when it had been a question of the knee condition. She had been treated outside the hospital for a contracted knee with a sinus. Her condition was poor, and she was underweight. There was a process in the knee, both constructive and destructive. There was a consistently negative blood Wassermann test. Dr. Coues said it did not necessarily follow that the eye condition was the same thing.

Dermatitis Herpetiformis. Presented by Dr. Faulkner.

A man, aged 47, a hotel clerk, three years before had had itching of the pubic region. He had thought it was a case of pediculosis pubis. After six months of itching, the condition spread over his entire body and cropped out in the form of vesicles. A skin specialist prescribed solution of potassium arsenite (Fowler's solution). The man had taken 15 drops three times a day, and when he was saturated, the eruption practically disappeared, except for a few lesions. The eruption appears, however, when the drugs are discontinued. The continued arsenic administration has produced marked hyperkeratosis in the hands and feet.

DISCUSSION

Dr. Faulkner said that phototherapy had been used for three or four days without improvement in the condition. He said the patient's teeth were in bad shape, several being capped. No roentgenogram had been taken.

Dr. Perry remarked that some similar cases had cleared up quickly after extraction of the teeth.

A Case for Diagnosis. Presented by Dr. Appel for Dr. William P. Boardman.

A white man, single, aged 25, whose family and past history was essentially negative, was first seen in the outpatient department five weeks before. About three weeks previously, he had first noticed a large red papule in the right iliac area. A day or two later, it became ulcerated. It soon became a superficial ulcer, round and itchy. Several days later, he noticed a crop of papules the size of match heads over his chest, abdomen, back and legs. These went through the same changes as the first papule, and soon his entire body was covered with these itching, red, raw, denuded areas.

Examination revealed a rather universally distributed, peculiar eruption, the lesions of which seemed almost all to be in about the same stage, although varying in size. The lesions were superficially ulcerated, some tending to be oval, others round, and showing evidence of scratching. Around the base of the penis and the scrotum, they were more maculopapular. Some of those on the back had a tendency to follow the lines of cleavage of the skin, but not so those on the arms or thorax. There was moderate enlargement of the inguinal nodes. The epitrochlear and auricular nodes were not palpable. The man's throat was essentially normal. He was admitted to the hospital. Pulse, temperature and respiration were normal. After some discussion, it was decided not to give him any specific treatment until the report from the blood test was received.

This was negative. Another Wassermann test was made later and was also negative, as well as a third. In the meantime, one of the enlarged inguinal nodes on the right was dissected out, and the pathologic report by Dr. Mallory was: "chronic inflammation; no evidence of syphilis."

The man received the regular sulphur ointment and hot bath treatment for scabies, with some relief and a partial clearing up of some of the lesions around the groin, but not much effect on the general picture. Some days later, several new lesions were observed on the right forearm; they appeared suddenly as bright red macular papules about 1 cm. square, somewhat itchy, and were soon covered with scales which were not thick or imbricated, although they left a bleeding surface when detached. During the past two weeks, Dr. Appel said that there had been a marked spontaneous progressive improvement. There was then hardly any itching, and the lesions showing the most pigmentation were the ones that were more ulcerated and had bled most. No lesions were present on the face and hands at that time. The case was presented for diagnosis.

DISCUSSION

Dr. Boardman said that the case had been a most puzzling one; that he had not felt that the condition was psoriasis, as it had not the right color nor the silvery white scale of psoriasis. Pityriasis rosea appealed to him as far as the arrangement went, but the color was not right. He thought the eruption had the character of psoriasis of some type.

Dr. Oliver said he thought that everything shown might be accounted for by scratching alone, and that the illustrations showed that the man had originally had pediculosis.

Dr. Smith asked Dr. Boardman to report his diagnosis on the case at the next meeting.

Dr. Perry said that some of the lesions made him think somewhat of a dermatitis factitia — a true artificial dermatitis.

Rhinophyma. Presented by Dr. C. M. Casselberry.

Dr. Casselberry said that he was not showing this case, that of a middle-aged man, as a matter of diagnosis, as he thought it was perfectly evident that this was a case of rhinophyma of about five or six years' duration. He had brought the case up first, because it was typical of the disease, and, second, because he wished to discuss the question of treatment, which he thought had been rather successfully worked out lately by surgical methods. Those who employed surgery had had more success in treating these cases than the others. He said good results had been obtained by excision, and apparently these cases do well without any skin grafting.

DISCUSSION

Dr. Oliver said that he had had a similar case two months before. The man was well satisfied with the result, and they had considered it good. There had been little scarring. Bleeding was rather profuse, but not alarming. Dr. Oliver said that he had used a thin bladed knife. He had had to tie up some little arteries. He had performed the operation under ether.

Dr. Perry told of a picture "before and after" operation, shown in one of the latest editions of Sutton, and remarked that if the present case could be given as good a result, the man should be very much pleased.

Dr. Boardman asked whether the usual treatment was just shaving?

Dr. Perry replied that it apparently was — that all the books on dermatology speak of it as "shaving the process off." He said he had done that once or twice, with good results.

Dermatitis Exfoliativa. Presented by Dr. Faulkner.

A young Greek, with a condition of four years' duration, had been in the hospital three times before. The first time, three years before, he had a red, weeping eczema, which progressed to a very dry, scaly form. He has never admitted receiving relief from any treatment that has been given him. He has had extreme itching. Last year he returned to Greece for three or four months; he thought that he felt better over there. The patient now presented a picture of exfoliative dermatitis. Dr. Faulkner said that they would be glad to receive suggestions as to treatment.

DISCUSSION

Dr. Clara P. Fitzgerald told of having treated a patient recently with lime water and chlorozene, with some success. The patient had had a good night's sleep while the cloths were wet.

A Case for Diagnosis. Presented by Dr. Loretta Joy Cummins.

A child had had scarlet fever in May and measles in June. The mother noticed skin changes early in June, about the time the child had the measles. When the child had been admitted to the hospital, about two weeks before, there had been marked keratosis of the palms and soles. There was no history of arsenic. The child had been given salicylic acid and sulphur, and the condition had improved somewhat under that treatment. The hands had been swollen and very much more irritated than the rest of the body.

DISCUSSION

Dr. Perry offered the diagnosis of keratoderma.

Dr. Cummins explained that before the child had had scarlet fever he had been very active, but that since then he had been rather dull. His hair had been falling out, and it was very dry.

Dr. Coues asked Dr. Cummins whether she did not think a little thyroid medication might help the child.

Dr. Cummins replied that she thought it might, but she had thought it best to have a metabolism test made first.

Dr. Perry noted that the child seemed to have a very large head.

Dr. Cummins said that the boy seemed rather heavy and stupid, but the mother had said that he had not been so before having scarlet fever.

A Case for Diagnosis. Presented by Dr. Henry J. Perry.

Dr. Perry said that the case was one from the Boston Dispensary. A man past middle life had had a peculiar lesion on the left side of his lower lip for six weeks. At one time when seen at the clinic the man had presented a distinctly eczematoid condition, slightly oozing and crusted, and on the inside of the lip there had been a small amount of leukoplakia. Dr. Perry said there was a possibility that it might be of the Paget's disease type. The man

had had an application of boracic acid ointment, which had cleared up a good deal of the crusting which the patient had presented. Dr. Perry felt that the man did not now look as much as though he had Paget's disease as he once had thought, and he had brought him in largely for diagnosis, as the condition on the lip was so unusual. Paget's disease of the lip has not been common, Dr. Perry stated, but a few cases have been reported in other places than about the nipple, and this raised the question of whether the condition was Paget's disease or an erythematous condition in a man who had smoked a good deal and who had held the pipe in this position.

DISCUSSION

Dr. Greenwood said that the condition was seen frequently in people who held tacks in their mouth, particularly lathers, and that he thought those cases that had been tested pathologically had turned out to be nonmalignant. Most of the patients had been treated successfully with radium. In this case, Dr. Greenwood said, he believed there had been no history of holding tacks in the mouth.

Dr. Perry said the man was a smoker. He commented on the process having been rather a rapid one.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 28, 1924

Hans Jorgen Schwartz, M.D., *President*

Kaposi's Sarcoma. Presented by Dr. Howard Fox.

A man, aged 53, born in Austria, a peddler, had lived in the United States for seventeen years. No member of his family, including his three children, had been similarly affected. The eruption shown began two and a half years before presentation as swellings of the right great toe and outer side of the left foot. Some of these lesions had been removed at the Essex Street Dispensary, and the remaining lesions gave him no trouble until three months ago, when the tumor masses began to enlarge, following the application of iodin. New lesions had also appeared on the hand a short time previously.

On admission to the Harlem Hospital Dispensary in August, 1924, he presented on the dorsum of the right great toe two soft fungating lesions, varying in size from one-fourth to one-half inch (from 6.3 to 12.7 mm.) in diameter and elevated about three-eights inch (9.3 mm.). The surface was raw and exuded serum. On the dorsum of the second toe and outer surface of the left foot were two pea sized, purplish, hard, hemispherical masses. On the dorsum of the right hand were three similar tumors, the largest being split pea sized. A histologic examination, made by Dr. F. Frank Fraser, showed the structure of a fibrosarcoma. The patient had been treated by the electro cautery, with considerable improvement.

DISCUSSION

Dr. Fordyce said that he agreed with the diagnosis. He said that the histologic picture depended on the part of the growth in which the section was taken; in some places the growth is purely cellular, while in others the vascular element is more pronounced.

Dr. Fraser said that he had recently seen several patients with this condition. He had been impressed with the fact that while they were typical of Kaposi's sarcoma from a clinical point of view, they showed great variation in their histologic structure. He had not observed any of those cases that had been reported as cutaneous angiomas. One patient who came under his observation showed clinically the condition of Kaposi's sarcoma, but the histologic picture was that of a granuloma. Whether some of these begin as granulomas, and in the course of development assume neoplastic features, is a question worthy of consideration. Dr. Ewing, in his textbook on neoplastic diseases, speaks of such a change. McLeod claims that Kaposi in his original description included a group of cases which were not sarcoma. Careful search in the present case revealed no evidence of angiomatous change. The structure was too cellular to be interpreted as fibroma. He would prefer, therefore, to call it a fibrosarcoma.

Dr. Fordyce inquired whether Dr. Fraser had ever seen any of the vascular spaces, to which Dr. Fraser replied that he had not seen them himself, but that his experience had been very limited.

Dr. Fordyce said that he had a series of photographs illustrating the various phases of the histology of the growth. Some of them showed a growth composed entirely of spindle cells, while in others there were venous sinuses lined with the cells of the tumor. This type of sarcoma differs from all others in that a primary tumor is not demonstrable. Furthermore, the clinical course of the disease is often very long.

Dr. Highman said he was surprised that Dr. Fraser had not seen the angiomatous phases of Kaposi's sarcoma, and told of a patient in whom he had once studied a series of lesions. The incipient lesions showed minute angiomas, the vessels and vascular spaces being surrounded by tissue which unquestionably was fibrosarcoma. As the disease developed, one found not only the early lesions, but others in the process of evolution and involution, partly lesions that could not be differentiated histologically from spindle cell sarcoma, and others that showed evidences found with any cell deterioration. As Dr. Fordyce said, the evolution is quite different from that of ordinary sarcoma, unless one conceives of it as a disease of the body as a whole with a tendency to multiple neoplastic changes. Gilchrist studied it and showed that the latest stages were pure sarcoma. This was not surprising when one considered that the same was true in cases of mycosis fungoides. Formerly, mycosis fungoides, sarcoma of Kaposi and xanthoma tuberosum were considered in the group of sarcoids showing the variations discussed. As Dr. Fordyce said, it all was a question of which lesion one studied.

Dr. Fox said that he would try to obtain another piece of tissue, and he hoped it might show the angiomatous element. He had enjoyed the opportunity of having Dr. Fordyce's sections demonstrated by Dr. Satenstein. They certainly showed the combination of angioma and sarcoma, characteristic of the disease.

Neurotic Excoriations. Presented by Dr. Howard Fox.

J. E., a man, aged 26, a jewelry broker, born in the United States, had suffered from an eruption for the last six years. It developed shortly after long service in the navy during the war and was situated on the face, scalp and forearms. He showed a few active lesions which were excoriated and crusted, and a number of pea sized superficial scars. The patient had previously been in a neuropsychiatric hospital.

ACRODERMATITIS CHRONICA ATROPHICANS. LICHEN PLANUS? Presented by DR. WISE for DR. FORDYCE.

A woman, aged 50, born in Sweden, married, came to the Vanderbilt Clinic on Oct. 28, 1924, for a condition on the hands and forearms which had been present for five years. The condition was worse in cold weather. On the flexor surfaces of both forearms were numerous pale red and brownish papules with a lichenoid appearance. There were patches of scaling erythema on the forearms and left elbow and on the dorsal surfaces of both hands. On the anterior surfaces of the knees and lower part of the thighs were large patches in which the skin was violaceous and slightly atrophic.

DISCUSSION

DR. LANE said that he could not be positive about a diagnosis, but that the lesions in the cubital fossae and in several other places alone were indistinguishable from lichen planus papules.

DR. KINGSBURY said he thought that the lesions were suggestive of two diseases, but were not definite in either case.

DR. HIGHMAN said he thought that the condition looked like dermatitis venenata.

DR. TRIMBLE said he thought that it was lichen planus, but not a typical case. Some of the papules were very small, but he would be willing to call the condition lichen planus tentatively.

DR. FORDYCE said that he would be willing to call the eruption on the forearms a lichenoid eruption but not lichen planus.

DR. CLARK said he thought that the condition was lichen planus. The lesions were typical shiny papules, and comparing that with the lichen planus papules seen on the patient with lichen planus of the penis and other lesions on the body, they were almost similar. He concurred in the diagnosis of lichen planus for the lesions on the arm.

DR. WISE said that he would try to submit a microscopic report on the case at the next meeting.

CIRCUMSCRIBED KERATOTIC HEMANGIO-LYMPHANGIOMA. Presented by DR. WISE for DR. FORDYCE.

A Russian Jewess, aged 39, married, eighteen years ago had a fatty tumor removed from the middle and outer side of the left thigh. Shortly after this operation a recurrence in the scar was noted, and for the last ten years the lesion had almost maintained its present size and appearance. The patch was about half-dollar size, irregular in shape, and made up of pinhead and larger bluish-red vascular tufts, most of which were topped with a keratotic or warty skin. The scar in which this lesion was located was hypertrophic, and showed some telangiectases in the vicinity of the warty vascular growth. A biopsy was refused. Angiokeratoma had been suggested as a diagnosis.

DISCUSSION

DR. LANE said that he agreed with the diagnosis.

DR. HIGHMAN said he thought it difficult to conceive of lymph as red. He could conceive of a lymphosarcoma with lesions as red as these, or hemangiomas and lymphangiomas. Dilated blood vessels impart a pink hue, but

nothing as deep as the red of these lesions. He did not think the case was pure lymphangioma circumscriptum.

Dr. Wise said he thought that Dr. Highman's points were well taken; most of these cases were hemangio lymphangioma, and he thought this was a case of vascular dilatation with lymphatic dilatation. There was probably a mixture, but he had little doubt as to the diagnosis.

Dr. Trimble suggested that the color probably was due to the previous operation, that section and anastomosis in the healing of the veins and small arteries might account for part of the appearance; it was a recurrence, and not the original lesion.

Favus. Presented by Dr. Howard Fox.

M. W., aged 20, a full-blooded negress, a native of South Carolina, had lived in New York for two years previous to examination. She was married but had no children. She had not come in contact with any one who, to her knowledge, had a disease of the skin or scalp. She had no domestic pets. The eruption was first noticed one month ago on the right arm, and two weeks later on the left arm. There were no subjective symptoms. On the outer aspect of the right arm she presented a circinate patch 3 cm. in diameter, the borders of which were slightly raised and showed minute vesicles. In the center of the patch were eight grouped yellowish cup-shaped, dry, crusted lesions, presenting the typical appearance of favus. On the inner surface of the left arm was a circinate lesion of the same size, with an erythematous center and finely vesicular border. It showed no crusts suggestive of favus. Several of the crusts on the right arm had been removed for microscopic examination, which showed the presence of mycelial threads. A culture was also made. She had received no treatment.

DISCUSSION

Dr. Fordyce said he did not think that any skin disease other than favus showed the characteristic cups. He believed the case was one of favus. One not infrequently saw on the body a single favus cup, surrounded by a scaling lesion which closely simulated tinea. He asked Dr. Fox whether an examination of the scales had been made.

Dr. Fox said he regretted that the eruption did not appear as typical as it did a few days before, owing to the removal of most of the crusts by traumatism. He felt that both of the lesions were due to the same organism. If one were favus, the other was the same disease. The lesion which was devoid of crusts could well have been the condition described as favus herpeticus.

Painful Nodular Lesion on Right Ear. Presented by Dr. Wise for Dr. Fordyce.

A man, aged 59, born in Russia, said that he had had recurrent lesions on the right ear for the last five years. The present outbreak began five weeks ago. On the upper margin of the ear were three nodules about buck shot size connecting with the cartilage. The underlying skin was thinned, and one of the lesions was absent. They were tender, and on the posterior surfaces of the same ear there was senile keratosis.

DISCUSSION

DR. FORDYCE said that the lesion on the back of the ear seemed to be an epithelioma. He had had considerable experience in the treatment of these, and the only successful method was the employment of the galvanocautery. The lesions would not then return.

DR. WISE said that a puzzling feature of the eruption was that the lesion on the back of the ear was not adherent to the cartilage. The patient's history was vague, but it was gathered that he had had this lesion only five weeks; it did not seem to have anything to do with the other condition, for the lesion was isolated and freely movable. A microscopic examination might prove it to be an epithelioma, and he would try to have this examination made and report the result at the next meeting.

FLAT EPITHELIOMA. Presented by DR. BECHET.

M. O., a woman, aged 33, from Dr. Williams' service at the New York Skin and Cancer Hospital, said that she had first noticed the appearance of the lesion when she was 29 years old. Since then, two more had developed, one as recently as two months previous to examination. The lesions occurred on the upper part of the chest and were extremely superficial, with considerable scaling and slight scarring in the center. The edges were slightly raised, rolled and pearly in appearance. The case was of interest because of the early incidence of the disease, the patient being 29 years old, and the fact that the lesions were so typical of this particular type of epithelioma.

DISCUSSION

DR. TRIMBLE said that it might be called Paget's disease, for it looked like that condition.

DR. G. H. FOX said that he had seen the patient as he came in, and was interested because he had that day scraped a similar lesion, an eczematoid disk, on a woman's cheek, which was undoubtedly epitheliomatous. In connection with what Dr. Fordyce had said about the galvanocautery and use of the curet, he wished to state that years before he had used the galvanocautery freely with Dr. Piffard, and had also used the curet, and had come to the conclusion that the cautery was more apt to destroy healthy tissue and leave a deeper scar. In scraping a superficial epithelioma with the curet, it must be done thoroughly or the operation would have to be repeated. The patient usually was told to return after a few months, and to report at intervals for a number of years to determine whether there was a recurrence. The disease was like a fire in the forest; if after extinction a single spark remained concealed beneath the leaves, it was likely to spread and the fire would become as bad as ever. At the present time, the curet did not seem to be used as thoroughly as it was years ago. If properly used, any superficial epithelioma could be easily and permanently removed, and it seemed, in his opinion, to be a better method of treatment than any other. A ring curet or a dental burr which would reach deep down into any cutaneous pocket might be used to destroy the diseased tissue, which was always softer than the healthy skin. If curettage is thorough, no cauterization of the wound is necessary.

DR. SHERWELL said that the curet had always been his favorite method for such cases, and he used it constantly. He was the originator of a method of using that in combination with mercuric acid nitrate. As Dr. Fox and

others had said, curettement must be used strenuously, and the treatment overdone rather than underdone. It made a favorable scar, and the patient would remain well. He had so treated a thousand or more such patients, and occasionally he met them in the street perfectly well after periods of twenty years or more. Of course it was not a neat operation, such as excision with the knife, but he had secured about 98 per cent. of good results, and was well satisfied with it. Some of the lesions had been very large, but most of them had been small. He curetted the lesions early and obtained good results. While his practice was not so large as formerly, he had operated on two patients during the last six weeks.

Dr. Bèchet said that his objection to using the term pagetoid in this particular case lay in the fact that the condition was not moist or eczematoid; on the contrary, it was essentially dry, with dry scaling and central scarring, with a typical rolled and pearly border, for which reason he preferred to call it a flat cicatricial epithelioma. With reference to the treatment, he would like to corroborate the remarks of Drs. George Henry Fox and Samuel Sherwell. The results of thorough curettage and cauterization with mercuric acid nitrate were exceptionally good. The cosmetic appearance of the scar was just as good, if not superior, to that following radiotherapy. This was particularly true in patients who have been treated with radium or the roentgen ray. In radiotherapy, it was easy to give an overdose, therapy causing subsequent disfiguring skin changes; in curettage and cauterization, the more thorough the treatment, the better the result. With the latter form of treatment, even in crateriform lesions, the resulting scar was soft, flat and pliable. As the two former speakers had emphasized, the secret of success lay in thorough curettage. He applied the acid full strength and did not neutralize it.

Acne Varioliformis. Presented by Dr. Howard Fox.

A man, aged 40, a clerk, born in the United States, presented an eruption on the face and scalp. About ten years before presentation, he had suffered from a similar condition, lasting for about eighteen months. The present eruption had first appeared about six months before. According to the patient's statement, the individual lesions appeared as "blisters," forming scabs which fell in two to three weeks, leaving scars. He presented a sparse eruption showing five active reddish, crusted, split pea sized lesions and pitted scars on the face and scalp. Some of the lesions suggested neurotic excoriations. Although the patient complained of some itching, he stated that he did not scratch and used no forceps or other instrument in the removal of the crusts.

DISCUSSION

Dr. Trimble said he thought that the condition was rather atypical.

Leprosy. Presented by Dr. Wise for Dr. Fordyce.

A negro woman, aged 33, married, born in the British West Indies, who had lived for six years in this country, had noticed the eruption for two months previous to examination. On the outer side of the thighs were quarter-sized, circumscribed, scaly and slightly infiltrated patches, with depigmented centers. On the upper part of the right arm there were three serpiginous, superficial and scaly lesions, also somewhat depigmented. A few small scars were to be noted in this area. The soles showed a scattered pea-sized macular pigmentation. All the leukodermatous areas showed a definite diminution of

sensation. The outer ends of the eyebrows were thinned, and the ulnar nerves were slightly thickened. There was no venereal history, and the patient had never been pregnant. Three Wassermann tests had been negative. Smears of the nasal secretion, even after taking potassium iodid, had been negative for the leprosy bacillus. Treatment was not instituted until confirmatory evidence from a biopsy and blood smear had been received.

DISCUSSION

DR. HIGHMAN said that the locality from which the patient came favored the diagnosis of leprosy; the appearance of the lesions was also somewhat suggestive; but in spite of these facts, he could not help thinking that the condition was a drug eruption of the phenolphthalein type, although there was no corroborative history. If it was not this, it could be nothing else than a neuroleprosy. Judgment would have to be suspended until the necessary studies were made.

DR. KINGSBURY said that he saw nothing to warrant the diagnosis of leprosy.

DR. TRIMBLE said he thought that the case was somewhat suggestive of leprosy, but that no one could make a positive diagnosis at the time.

DR. WISE said that he had not reported the case to the Health Board as leprosy, pending a histologic report; but he felt sure the patient would bear watching, for she had a spot of leukoderma on the wrist which was suggestive. A report of the laboratory findings would be submitted at the next meeting.

LICHEN PLANUS HYPERTROPHICUS. RESULTS OF TREATMENT WITH MERCURIC SALICYLARSENATE. Presented by DR. BECHET.

A man, aged 56, born in Italy, said that the lesions had been present for a year and seemed unaffected by treatment. When he appeared in Dr. Aitken's service four months previously, he had a large number of rounded, markedly thickened, wartlike, dark purplish lesions on both legs. There were typical irregular quadrangular, violaceous, shiny lesions on the forearms. Since the first visits the patient had been most irregular in attendance. He had received only six intramuscular injections of mercuric salicylarsenate, yet improvement was most marked after the first two injections, and after the sixth the lesions had disappeared, leaving only the usual pigmented stains so commonly observed after involution of the lesions.

DISCUSSION

DR. FORDYCE said that it was a remarkable result and worthy of being followed up, for these conditions were occasionally obstinate.

PITYRIASIS LICHENODES CHRONICA. Presented by DR. WISE for DR. FORDYCE.

A boy, aged 7 years, born in this country of Russian Jewish parents, had an eruption of six months' duration, which was generalized over the trunk and scalp. It presented pinhead and larger sized papules that carried a fine scale which was rather adherent and left no bleeding points on removal. The flexors as well as the extensor areas were involved. A pea sized leukoderma was present on the neck. There was no itching, and the boy was in good health. A biopsy was refused. The patient was being treated with general body irradiations from the ultraviolet ray lamp (Alpine light). No improvement was noted.

DISCUSSION

Dr. Fordyce and Dr. Trimble said that they agreed with the diagnosis.

Dr. Howard Fox asked whether any one had had any experience with phototherapy, as suggested by Dr. Chipman, who had reported a case of parapsoriasis that cleared up under ultraviolet light treatment.

Dr. Bechet, replying to Dr. Fox's question, said that some years previously he had treated an extensive outbreak of the disease with the mercury quartz lamp. The treatment had been most energetic, and had been pushed to the point of severe reaction. The results had been extremely good, but unfortunately proved impermanent, the eruption recurring to some extent.

Dr. Lane referred to the case of a medical student, whom he had presented before the Society some six months previously, with a marked case of this disease. This summer the young man worked outdoors, stripped to the waist. When seen this fall the eruption on the rest of the body was as marked as ever, but the upper part where it had been exposed to the sun was perfectly clear. The improvement however, probably would be only temporary.

Dr. Wise spoke of a patient with pityriasis lichenodes chronica, who was treated by Dr. McCaskey with intensive ultraviolet light reactions, and apparently was cured.

Psoriasis in a Mulatto. Presented by Dr. Howard Fox.

C. L., a woman, aged 28, born in the United States, a mulatto, had first noticed the eruption eight years previous to examination. The condition consisted of a small number of dry, thickened, reddish patches covered with silvery scales. These were situated on the elbows and knees. The patient had previously been treated by a dermatologist of another city for psoriasis. She was of robust appearance.

Dr. Fox said that while not a great rarity in negroes with an admixture of white blood, nevertheless psoriasis was uncommon in such persons. It was extremely rare to see the disease in a full blooded negress, such as the patients presented by Dr. Parounagian and the speaker in New York during the last year.

Report of Culture of Ringworm of the Scalp in an Adult. Presented by Dr. Howard Fox.

A negro, had been shown before the Society on May 27, 1924. On that occasion there had not been sufficient time to learn the result of cultures, though the microscopic examination of pus (the lesion being a kerion) had been positive. Cultures on Sabouraud's glucose agar showed a growth which was rapid, pure white and downy, consisting of central, somewhat convoluted masses with a narrow interlacing border. The cultures had never shown any tendency to become pleomorphic. The picture presented by the hanging drop preparation showed mycelial threads, numerous small spores without particular grouping in clusters mostly detached from the mycelium and, in addition, a moderate number of large round spore-like bodies scattered free in the preparation. No fusiform bodies, spirals, or thyrses were seen. A diagnosis of *Trichophyton* (niveum) *radians* was made.

H. Schuyler Clark, Secretary.

MINNESOTA DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 5, 1924

G. M. OLSON, M.D., *Presiding*

LUPUS ERYTHEMATOSUS. Presented by DR. SHAPIRO.

Mrs. J. S., aged 29, married, had had the condition for two years. The lesions were located on both cheeks, also on the bridge of the nose all the way down to the tip, and extended laterally both right and left, especially on the outer edge of the lesion was wrinkled and atrophic. The lesion started brane was not involved.

The lesion on the left cheek was semicircular, about 2 inches (5 cm.) in one direction and three-quarters inch (1.9 cm.) in another. It was rough to the touch and raised from the surrounding skin. The border was sharp, definitely outlined and markedly palpable in contrast with the surrounding skin. There were no isolated lesions; they all appeared to be confluent. The skin was reddened and appeared to be infiltrated. It was covered for the most part with large, coarse and closely adherent scales. A similar condition existed on the nose, only that this lesion was more crusted than the other, and it was verrucous. This lesion was the older of the two. The skin was reddened in places, and in other places there was nothing but hard, horny scales, closely adherent to the underlying tissue. In other places there was scarring, with slight atrophy of the skin, but no telangiectasia. Near the right eye, the skin was very much infiltrated, blood red and hard to the touch.

The patient has a left tuberculous cervical adenitis. She seems to be making some improvement under roentgen-ray therapy, in one lesion especially. The other is still covered with thick scales, and not much improvement has taken place in that. Dr. Shapiro stated that he would like suggestions as to therapy.

DISCUSSION

DR. BUTLER said he did not believe that one ever made progress treating these patients with roentgen ray. He said that he had a case almost similar to the one under discussion. The patient was doing very well under treatment with radium applications, and Dr. Butler thought radium much superior to the roentgen ray. He was of the opinion that better results would be obtained in this case by freezing the lesions with carbon dioxid snow.

DR. SWEITZER said he felt that Dr. Butler's remarks should be emphasized, for in the treatment of lupus erythematosus if a dose of roentgen ray strong enough to remove it is used, one would probably get a burn. Dr. Sweitzer said that he would advise freezing and refreezing it, for he felt that a much better looking result would be obtained by this method.

DR. NORMAN WALKER said that he had never seen carcinoma following lupus vulgaris that had not been treated profusely by the roentgen ray.

DERMATITIS HERPETIFORMIS GESTATIONIS. Presented by DR. SWEITZER.

Mrs. H., aged 20, eight months pregnant, had a bullous eruption on an erythematous base on both forearms. The eruption itched and burned. A previous pregnancy was followed by a similar eruption. The present eruption started two months before presentation.

The patient consulted Dr. Sweitzer a week before presentation, and he thought the case was one of dermatitis herpetiformis. The history of the

eruption having occurred in each previous pregnancy, followed by periods of freedom, and starting again during this pregnancy, led him to make a diagnosis of dermatitis herpetiformis gestationis.

A Case for Diagnosis. Presented by Drs. Irvine and Turnacliff.

A man, aged 78, presented a lesion the size of a quarter in the middle of the lower lip. According to the history, the lesion started in June. The edge showed neither infiltration nor a pearly border, but instead appeared like some warts, as though it could be pressed out of a capsule. The surface was rough, and sebaceous material could be expressed, appearing between the warty prominences. It bled easily. No glands could be palpated.

Clinically, it was a seborrheic wart. A biopsy showed no carcinomatous tissue, but unfortunately was not sufficiently deep to make a conclusive statement. Final diagnosis would have to depend on the microscope.

DISCUSSION

Dr. Felden said that the plainly palpable deep infiltration underneath the growth made a diagnosis of epithelioma more probable than merely of a wart. The fact that the raised border was lacking, which sign is pathognomonic only for basocellular epitheliomas, and the fact that the lymph glands were clinically intact do not decide against the diagnosis of epithelioma, because this verrucous proliferative type, histologically classified under squamous cellular epitheliomas, usually remains relatively benign for a considerable time.

Dr. Butler said that he did not think this lesion was an epithelioma, but, if it was, he thought it was one of the squamous cell type. He felt it would be a good case for radical treatment and section. He did not think it was a squamous cell epithelioma at the present time.

Dr. Irvine said that of course the final diagnosis rests entirely with the microscope. The lesion was growing rapidly, and so far as he could learn from the history, there was no lesion there until June. Dr. Irvine was of the opinion that if the man had squamous cell epithelioma which grew as fast as that, the glands would be involved, and apparently they were not. The edge of it appeared to him to be very much like that of some plantar warts. Clinically he would make a diagnosis of verruca, or, if pus were present, granuloma pyogenicum might be considered. He had made a biopsy, but Dr. Bell said that it was not distinct enough to make a final statement, although no carcinoma was seen in the specimen.

Dr. Michelson said that his clinical diagnosis was epithelioma. He would consider verruca vulgaris and pyogenic granuloma merely to exclude them. Size alone would rule out the diagnosis of wart. The only warts that he had seen that approached this one in size were those which occasionally followed impetigo. Last year he had seen a patient who had impetigo on both legs, and several months later the patient had multiple warts, many of them as large as half a dollar.

As for pyogenic granuloma, dermatologists looked on this as a pedunculated lesion, but general pathologists diagnosed pyogenic granuloma in many cases in which there was no pedicle. Dermatologists also had a different view than pathologists as regards the microscopic picture of pyogenic granuloma. Dermatologists looked on the lesion as one made up largely of angiomatous tissue with infiltrate and covered with frayed-out, or very much thinned,

epithelium. The pathologists, on the other hand, included tissue which was made up largely of cellular infiltrate with some new vessels and marked acanthotic change in the epidermis.

As regards treatment in this particular case, Dr. Michelson thought a "V" excision was all that was necessary, because the patient was well advanced in years, and there was apparently no involvement of the drainage areas. He did not think that a man of this age should be subjected to the radical operation.

Dr. Olson said that Dr. Wright some years ago showed a few cases of this type of wart. He made a point at that time that a lesion of the lip that you could squeeze out, as though it were in a sac, was not epithelioma but a wart. Dr. Olson said that he had made sections from three cases of granuloma pyogenicum of the lip that looked very much like this case — the top smaller than the bottom. In epithelioma, the lesion at the bottom is smaller than at the top, or, at all events, it does not show a saclike form.

The lesion in his patient was a very large one, and the diagnosis would depend on the biopsy.

Dr. Irvine said another thing that influenced his diagnosis was the statement made by Bloodgood two or three years ago, that out of the last 500 lesions he had removed from the lower lip, on careful microscopic study, 50 per cent. proved to be warts.

Dr. Olson said that he agreed with Dr. Irvine. Two cases in which sections had shown granuloma pyogenicum of the lip had been diagnosed as epithelioma by a number of very good surgeons.

Dr. Sweitzer said that he thought this would be a good case in which to have photographs taken. He would guess that the condition was carcinoma, but he might be wrong. He said that a large percentage of epitheliomas of the lower lip are not very malignant and are cured by a V-shaped incision. Sometimes, however, they are very malignant.

Dr. Olson said that one division of carcinoma is malignant wart.

Dr. Michelson said he thought that was a papillary type of epithelioma.

Scleroderma en Plaque. Presented by Dr. Shapiro.

Mrs. R. M. S., aged 60, a widow, presented a lesion in the right lumbar region of thirty years' duration. The lesion was about 4 inches (7.6 cm.) long and one and one-half inches (3.8 cm.) wide. It was fairly well differentiated from the normal skin. It was extremely hard to the touch, and the skin appeared to be under tension; also it had a dry feel. The color of the lesion was white on the extreme edge; then a rose red appeared toward the middle, and it became more intensely red as we approached the center. This extreme red color could be removed under pressure. Some of the redness was due to the telangiectasis, which, in turn, was probably due to therapy. The extreme center was ulcerated. The ulceration was not deep, and the floor of the ulcer was whitish gray and clean. The edges were rough, irregular and quite hard to the touch. The skin on the outer edge of the lesion was wrinkled and atrophic. The lesion started thirty years ago. It was small at first and occupied the area that is the center of the present lesion. It did not grow until about six years before presentation, when the patient took up her residence in the West Indies. She had received a good deal of quartz lamp therapy and also roentgenotherapy. The ulceration occurred prior to radiation treatment.

The patient had recently had her tonsils removed. Her metabolism was minus 27.

DISCUSSION

DR. SHAPIRO said that if the ulceration had occurred after roentgenotherapy, he would think it was an roentgen-ray burn, but, according to the patient's statement, it came before. He thought the condition was scleroderma.

DR. FREEMAN said that if the ulceration had appeared before the roentgenotherapy that would certainly rule out roentgen-ray burn. He said the patient had plenty of loose tissue around the lesion, and his suggestion would be to excise the whole region. He felt that the condition was scleroderma.

ECZEMA. Presented by DR. FREEMAN.

Dr. Freeman presented a patient who had generalized eczema, in order to obtain some suggestions as to therapy.

DISCUSSION

DR. SWEITZER said that he had been interested in the therapy of this type of eczema, and in some cases had obtained good results by giving small doses of foreign proteins in infinitesimal doses. He had used the German method. He gave alcohol, 0.1 c.c. diluted with distilled water up to 1 c.c.; then 0.2 c.c., and 0.3 c.c. and spread the time to three days, and then gave 0.4 c.c. Some good results had been obtained, and some cases had cleared up well.

He had also used formic acid in dilutions of 10, 11 and 12; that is, 1 part formic acid to 10 parts of water, then that diluted to the tenth and twelfth dilution. He gave this about once a week. He recently had a case from St. Paul in which the patient had been treated with the roentgen ray and lamp for six months. This patient had eczema on her elbows, hands, flexor surface of the arms and on the legs and chest for more than a year. She had received no treatment since but boric ointment and formic acid, and the eczema had just about cleared up.

In these cases, Dr. Sweitzer felt that the first few injections seem to do more good than the ensuing ones. In this particular case, the crusts fell off profusely.

Dr. Sweitzer said that he had also tried the foreign protein treatment in psoriasis, using no salve, and sometimes the patients had lost 75 per cent. of the scales in a little while.

A CASE FOR DIAGNOSIS. Presented by DR. FREEMAN.

Mrs. D., aged 26, had a lesion behind the right ear. It began as a small nodule one year before presentation, gradually spread peripherally into the present lesion, which was nodular in character, deeply infiltrated, sharply defined, of cartilaginous hardness, and about the size of a five-cent piece, with borders elevated. The telangiectasia was due to treatments with carbon dioxid, which caused improvement but not cure. The lesion appeared to be granuloma annulare.

DISCUSSION

DR. IRVINE said that he thought the condition was an epithelioma of the morphea type.

DR. BUTLER said that Dr. Freeman said this patient had had the lesion only since May, and Dr. Butler thought from its size the growth was too rapid for a basal cell epithelioma. He thought the freezing Dr. Freeman

had given it should have cleared it up. His impression was that it was a hypertrophic scar. There was new vessel formation, but the vessels did not extend over the border as in true basal cell epithelioma. The sclerotic condition extended into the middle of the lesion, and made him feel that it was a keloid or hypertrophic scar.

DR. SWEITZER asked what the lesion looked like before it was frozen.

DR. FREEMAN said that it looked practically the same as now, only the lower border was not nearly so pronounced as it had been, and the telangiectasia had disappeared. It was frozen twice, five minutes each time, but there was no ulceration.

DR. MICHELSON said he thought that a biopsy was necessary in this case in order to prove the diagnosis conclusively. He felt that clinically this was a basal cell epithelioma, and would predict that the microscope would show it to be cystic in type. At the edge, the lesion was made up of globules, translucent in appearance, with minute dilated vessels running over the surface. He thought the treatment of choice would be radium exposures.

(NOTE.—Dr. Michelson examined the biopsy the next day and reported that the section showed that type of epithelioma which had both squamous and basal characteristics, the so-called cancer-mixte of Darier.)

DISCUSSION

DR. OLSON said that his impression was that this was a basal cell epithelioma of the cylindroma type. This sometimes grows over the scalp. He recalled a case seen with Dr. Sweitzer, that of a young lady who had a tumor very much like the present one, which grew as large as a saucer over the top of the scalp. Some of these tumors involve the whole scalp. Microscopically, they are basal cell epitheliomas. They seem to grow under rather than in the skin.

DR. SWEITZER said that that type (growing over the whole scalp) is the cystic type of basal cell epithelioma. He said he had treated the patient Dr. Olsen had mentioned by excising it and performing a skin graft. He then treated her with radium, and thought the condition was cured. Later it seemed to spread by the lymphatics, and grew slowly around her head. Dr. Bissell gave her roentgen-ray treatments. Dr. Sweitzer knows that she is still alive, but he has not seen her for some time.

Recently he had a patient, a young man, with a lesion on the side of his nose which looked almost like this only smaller. This grew rapidly. A biopsy showed cystic epithelioma.

DR. SWEITZER said he thought this case of Dr. Freeman's was basal cell epithelioma.

DR. OLSON said he thought this patient would show a typical basal cell epithelioma.

DR. SWEITZER said that he would use the cautery first and flatten the lesion down pretty well with that, and then use radium. He thought that would remove the growth permanently. He would give the radium for about six hours, unscreened, with a 10 mg. plaque.

DR. COOK asked what the idea was in using the cautery.

DR. SWEITZER said that one could kill off a lot of tissue with the cautery and the radium then acts on the deeper cells. He said he preferred using cautery first and then the radium.

LATER REPORTS ON CASES FROM OCTOBER MEETING

A Case of Granuloma Annulare (?) in a Girl Aged 14 Years, Dr. Michelson.

Dr. Michelson said that all of the lesions had completely disappeared without any treatment, and that precisely a month from the day shown she returned with lesions just beginning to appear again. Although there was no direct relation to menstruation, still there was no doubt about the cyclic character of the eruption, which would make Dr. Michelson tend toward the diagnosis of symmetrical dysmenorrheic dermatitis.

A Case of Seborrheic Dermatitis. Dr. Michelson.

Dr. Sweitzer said that this man had received such good treatment before he came to the hospital that they had a hard time deciding what to do. He had received phototherapy and treatment with various ointments. Dr. Sweitzer had tried treatment with alcohol on the patient, which apparently had not been effective; he then started to use formic acid. The patient's whole body had been red, and within a week one could see clear skin, but the face and neck were still much involved. He then gave the patient the same sized dose the next week, and he had a relapse. The fourth dose was given the Monday before presentation, and at the present time the body, arms, and legs are about 75 per cent. healed. The body is in very good shape, but the neck and face are badly involved. Dr. Sweitzer said that he understood the patient did not tolerate ointment therapy very well, and they had not tried that.

D. D. Turnacliff, M.D., Secretary.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 10, 1924

Edward F. Corson, M.D., *Presiding*

Majocchi's Disease. Presented by Dr. J. M. Schildkraut (by invitation).

A man, aged 41, a foreman in a linoleum plant, ten years ago developed a red, itchy blotch on the inner side of the leg, just below the knee. New spots appeared, gradually fused and became pigmented. The blotches now covered both legs. The border was sharply marginated, somewhat reddish and purpuric. About two years ago, the spots began developing on the body, and during the last two months they had appeared on the arms. The condition did not annoy him in any way, and there was no induration in the patches. In 1919, the patient developed typhoid fever, and the condition temporarily disappeared.

DISCUSSION

Dr. Jay F. Schamberg stated that this case was rather difficult to classify. The patient had pronounced pigmentation in the oldest areas — other areas were reddish with evident capillary dilatation, which ultimately disappeared, leaving the pigmentation. In some places, there was slight evidence of atrophy. The suggestion of Majocchi's disease was pertinent, but the symptomatology did not fit in. Some of the patches on the body suggested parapsoriasis, but those on the legs did not. Those on the legs suggested the disease described

some years ago as progressive pigmentation of the skin. However, this case could not easily be put in any particular category.

Dr. F. D. Weidman suggested the possibility of atypically distributed changes similar to those of Majocchi's disease, and recalled a case in which the only patch was located over the right thigh and would have been called Majocchi's disease but for the atypical distribution. The basis of Majocchi's disease was evidently some disturbance of the circulatory system, and this case would call for a painstaking internal medical examination.

Lupus Erythematosus. Presented by Dr. J. M. Schildkraut.

A white woman, aged 50, when 8 years old had had erysipelas, following which an erythematous patch had formed on the right cheek, remaining dormant until ten years ago. The blotch then spread over the face and scalp; and last summer it developed on the arms.

DISCUSSION

Dr. John H. Stokes agreed with the diagnosis, and asked whether or not the patient had shown symptoms of acute dissemination or arthritic manifestations. But since the patient had worked every day, she had apparently been in good health. Deep roentgen-ray therapy was suggested for treatment, as apparently it had helped in some cases, although in other cases it had not been beneficial. However, it seemed that the less one did apart from established measures the better these patients got along.

Dr. Jay F. Schamberg quoted the cases of three patients whom he had successfully treated three years ago by the method used at the Mayo Clinic. But he advised careful watching of the patient because of the possibility of an acute flare-up. One of his patients developed intense sunburn last summer, and showed widespread lupus erythematosus on the back and forearms on what previously had been the seat of the solar burn. He was sent to the mountains and came back with improved health. Patients had been seen in an acute exacerbation, with fever, pneumonic consolidation ending in death; some with evidences of nephritis; others with chronic pulmonitis, which may have been of tuberculous nature. But there had not been a sufficiently large number of cases with careful necropsy findings to give a concrete picture.

Dr. F. D. Weidman called attention to the rather remarkable distribution in the case presented: the lesions were on the exposed portions of the body and on the anterior surfaces of the upper extremities, like an erythema multiforme; and he suggested that the effect of trauma and exposure may have had something to do with the effects of the disease. He suggested also the possibility of there being a circulatory factor probably soluble in character rather than bacterial.

Psoriasis. Presented by Dr. Edward F. Corson.

A. K., a post-office employe, aged 26, presented an eruption suggesting psoriasis, but it was located on the genitalia, axillae, scalp and around the umbilicus. Attention was called to the unusual situation of the outbreak.

DISCUSSION

Dr. John H. Stokes recalled a patient shown at St. Louis in whom the eruption was thought to be psoriasis by everyone present; but a parasitic fungus was found on examination of the scales.

ERYTHRODERMA SUPERIMPOSED ON ICHTHYOSIS. Presented by DR. J. M. SCHILDKRAUT.

A man, aged 56, a night watchman, born with a dry scaly skin, apparent ichthyosis. He had a sister, aged 43, with the same condition. She was epileptic. Last summer the patient developed an erythroderma which was persistent. He complained of the itching. There was marked keratosis, on the palms, with thinning on the fingers. The same condition prevailed on the feet.

DISCUSSION

DR. CARROLL F. WRIGHT asked whether a differential blood count had been made, and quoted a case in Ann Arbor which showed the same condition, with the addition of an enlarged inguinal gland. That patient had 60,000 white blood cells with lymphocytosis, and was reported as having a case of leukemia cutis.

DR. JAY F. SCHAMBERG called attention to the history of the case and to the fact that commonly a secondary process of inflammatory nature may be imposed on an ichthyosis. It was possible that the patient, through trauma or something which brought about increased circulation of the skin, had developed a chronic inflammatory condition. There were some cases of erythroderma which later showed blood changes, but the case presented should be regarded as an erythroderma superimposed on an ichthyosis.

BROMID ERUPTION. Presented by DR. J. V. KLAUDER.

A woman, presented a typical bromid eruption, but on discontinuing the drug, of which she had been taking rather large doses, the lesions involuted. About four months after the last ingestion of bromid a new crop appeared. She had been taking a proprietary asthma cure for fourteen years, which probably contained iodids.

DISCUSSION

DR. EDWARD F. CORSON stated that clinically the condition appeared to resemble a bromid rather than an iodid eruption.

DR. JAY F. SCHAMBERG agreed with Dr. Corson. Commonly these eruptions begin as blebs, vegetations growing underneath the epithelial surface, later the roof of the bleb is cast off. Such conditions have been mistaken for smallpox and for pemphigus. Characteristic of this type is the late date at which a new eruption may take place after the ingestion of the bromids has been stopped.

EPITHELIOMA FOLLOWING APPLICATION OF ROENTGEN-RAY TREATMENT FOR EPILATION. Presented by DR. W. S. NEWCOMET (by invitation).

A white woman, German, aged 39 years, received roentgen-ray treatments fifteen years ago for the removal of hair from the arms. The patient had been treated by many physicians both here and in Germany. About one and one-half years ago, she presented a roentgen-ray dermatitis of both arms, with breaking down of the skin. She was treated with an astringent dressing powder and cautery. She then went to Germany, where she was given the "sun" treatment. The only remaining ulcer was now several times as large as one and one-half years ago. In addition, several small areas were becoming malignant.

DISCUSSION

Dr. G. E. Pfahler suggested that the best treatment was to destroy the entire area by electrocoagulation, and allow healing by granulation or skin graft. He called attention to the dangers of the roentgen-ray, especially because of the idiosyncrasies of the various skins to the rays. He quoted experimental work done on mice, in which variations of 100 per cent. occurred, although the animals used were of the same litter and subjected to the same strength of radiation. Hypertrichosis must be treated very carefully, as it takes very delicate measurement to deliver just the amount of radiation which will kill only the hair bulbs.

Dr. F. D. Weidman stated that this patient was seen by him two years ago, and the diagnosis of epithelioma made, with recommendation that the lesion be excised. Biopsy was made at that time, and as the lesion was now at least a dozen times larger than it was at that time, the question as to the advisability of making biopsies short of actual excision becomes pertinent. He quoted the experimental studies of Dr. Carter Wood, in which it was found that the expectation of life was just as long in the animals in which biopsy had been made as in those in which it had not been made; but, on the other hand, massage of the tumors tended to induce earlier metastasis. He asked concerning the advisability of radiation of the axilla for superfluous hair.

Dr. Jay F. Schamberg agreed with Dr. Pfahler as to the therapeutic procedure to be followed in this case, and endorsed the statements as to the variability in reaction of different persons to radiation, particularly from radium, if the radium substance is used. It has been noted, especially in children, under identical conditions of treatment, that idiosyncrasy was wide. Dr. Schamberg did not advise the use of radiation for the treatment of any simple cosmetic deformity unless it constituted a deformity of such extent as to render the patient socially and mentally unfit. He urged cooperative research to devise better technic for the treatment of cosmetic deformities, such as hypertrichosis and scars.

Hemophilia and Multiple Angiomas. Presented by Dr. W. S. Newcomet.

A white woman, aged 56, was referred for treatment of nose bleed. She complained of the bleeding, particularly at night. She controlled it with cotton. Her mother and her mother's father were bleeders. The father died of kidney trouble and the mother of heart disease. She had three daughters, two living and well, with no trouble of this nature. Menses began at 14, regular at twenty-eight day intervals, quantity free, no pain. Deliveries had not been difficult. There was no bleeding of any passages, no large veins, and no trouble with urination. Laryngoscopic examination of the throat showed an irregular palate; otherwise the examination was negative. There was some destructive process involving the soft palate; the uvula was entirely eroded, and there was blood-stained mucus coming from the pharynx. The Wassermann test was negative; it was reported to have been four plus four years before. Blood examination revealed: hemoglobin, 35 per cent.; red blood cells, 2,250,000; white blood cells, 4,600; polymorphonuclears, 57; lymphocytes, 27; large mononuclears, 12; transitionals, 4; coagulation time, four minutes. The blood was Type IV. Direct transfusion was given, with much improvement. Radium was advised. Small angiomas were to be seen on all the visible mucous membranes of the body, including the tongue. There was also an eruption on the legs. The mother had a similar eruption.

DISCUSSION

Dr. Jay F. Schamberg noted that the appearance of the throat was distinctly syphilitic, but questioned whether or not the hemorrhagic condition could be linked up with syphilis. Syphilis itself might lead to a capillary degeneration with a formation of capillary aneurysms.

Dr. John H. Stokes had reported a case of syphilitic telangiectasis, but stated that the case presented did not fall into that class. The syphilitic type is much more diffuse. There was a syphilitic and a nonsyphilitic group which were practically indistinguishable. These patients almost invariably apply for treatment of the hemorrhage from the nose.

Dr. G. E. Pfahler reported a case seen by him, with repeated nasal and rectal hemorrhages associated with multiple telangiectases. The Wassermann reaction was negative on repeated examination. The literature had contained two reports recently on the treatment of such conditions. One reported case showed hemorrhages chiefly from the uterus. The patient was given radium in the uterus, and at the same time the spleen was irradiated with the roentgen ray about once in two weeks, approximately one-tenth erythema dose being used each time. The effort to control these cases of hemorrhage by stimulating doses of the roentgen ray over the spleen has been more or less successful.

Psychic Hyperhidrosis of the Palms and Soles. Presented by Dr. J. V. Klauder.

A young white man, a draftsman, complained of excessive perspiration of the palms and soles. He was treated by the roentgen ray, 1¼ erythema dose being used; later he was given 1⅛ erythema dose. After this it was noticed that the patient would walk into the office with the palms perfectly dry, and within a few seconds they would be dripping water. His emotions were so unstable that the palms could be made almost dry or wet at will. There was a psychic element in the case—the patient had distorted views of the physiology of the sweat mechanism, and had an element of phobia, fearing a condenser and getting the excessive perspiration when working with it. Psychotherapy was tried, and had caused improvement. However, the fact that the roentgen-rays were used must be taken into consideration.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, Nov. 11, 1924

Paul E. Bechet, M.D., *Chairman*

Dermatochondritis Nodularis Helicis. Presented by Dr. Wise.

This case was previously presented before the New York Dermatological Society, Oct. 28, 1924.

DISCUSSION

Dr. Fraser said that he had seen the case when presented before the New York Dermatological Society. At that time, the lesion on the back of the ear was suggestive of epithelioma. He still believed it to be epithelioma. He then inquired of Dr. Wise whether any treatment had been given since the case was shown in October.

DR. SCHEER said that no treatment had been given.

DR. LEVIN said that he had presented this patient before the Section about three years before, and the diagnosis was confirmed at that time. He had not seen the patient since. The new lesion on the back of the auricle seemed to be a senile keratosis and was possibly epitheliomatous.

GRANULOMA INGUINALE. Presented by DR. THORNLEY.

J. D., aged 29, a seaman, born in the United States, had been presented about a year and six months before. He had received eighty-one injections of tartar emetic (10 c.c. of 0.5 per cent. solution).

DISCUSSION

DR. GOODMAN said the statement that eighty-one injections had been given was not indicative of the therapy. One would like to know the dosage and the interval between the injections. It was possible to keep the patient on the same dose, about 5 c.c. of a 1 per cent. solution, or to increase the dose gradually to about 12 c.c. He had never given more than the latter, and then he had to dilute to about five times the amount with distilled water, because the patients complained of pain at the shoulder of the arm into which the injection was being administered. The clinical result of treatment in the case presented was excellent. The possibility of recurrence was not to be disregarded, however, and prophylactic treatments of tartar emetic intravenously should be continued. Dr. Goodman said that he would like to take the opportunity of speaking of another use for tartar emetic solution in therapeutics. Since his tropical and temperate zone experience with tartar emetic in granuloma inguinale, it had occurred to him to try the solution in another ulcerative condition, namely, chancroid. His experience up to the present time had been favorable enough to convince him that it was worthy of further trial. In clinical cases of chancroid with negative dark-field findings for *Spirochaeta pallida* and Donovan bodies, and a negative Wassermann test, he had administered the tartar emetic intravenously as he would in a case of granuloma inguinale. The initial dose would be 5 c.c. of the 1:100 solution. The dose would be given as often as every second day, or at longer intervals, to once in four or five days. The number of injections had been as low as four, with eight as the highest number in one patient. Local cleanliness of the chancroid lesion was a concomitant.

DR. ABRAMOWITZ said that he had seen the patient before, and the result under treatment was excellent; but in many instances there were recurrences as soon as the tartar emetic treatment was discontinued. Recently, at the International Conference on Health Problems, held at Jamaica, Castellani reported satisfactory results with injections and local applications of phosphorus oil of the British Pharmacopeia, in Oriental sore, and he also advised its use in granuloma inguinale (J. A. M. A. **83**:1192 [Oct. 11] 1924).

DR. FOX considered the therapeutic result excellent in this case. While tartar emetic was entitled to be called a specific in granuloma inguinale, its action was slow. This had been proved by his experience that many injections of the drug were needed to obtain successful results.

DR. PAROUNAGIAN had seen a number of these cases and was very much encouraged by treatment with tartar emetic. In most cases, however, recurrences occurred.

Dr. Thornley said that the case had been presented before the Section previously; that Dr. Satenstein, as well as the pathologist at the U. S. Marine Hospital No. 70, had found an organism closely resembling the Donovan body; that repeated Wassermann tests were negative; and that scrapings injected into a guinea-pig had given no evidence of tuberculosis. The treatment consisted of intravenous injections of tartar emetic in solution, beginning with 0.1 per cent. and increasing up to 0.8 per cent., when pain in the shoulder and distressing cough were experienced by the patient. The dose was then reduced to 0.5 per cent., and thereafter this dose was administered twice a week for almost a year, without any unpleasant symptoms. There was marked improvement for a time, but later the condition seemed to become stationary. Electrical coagulation of the granulating areas was then supplemented to the intravenous treatment, with complete cicatrization as shown.

Mycosis Fungoides. Presented from the Vanderbilt Clinic by Dr. Abramowitz.

G. K., a Russian Jew, aged 60, married, had suffered from a severe itching eruption for one year. He was referred to Gouverneur Hospital Dispensary for a biopsy. He presented palm-sized and larger, livid, red plaques that appeared as rings and segments of a ring, some festooned and some with circles within circles. All the lesions showed infiltration, particularly at their edges, and a tendency to fade and reappear. The eruption involved the whole body, including the scalp. Several examinations for fungi were negative. Roentgen-ray treatment was evidently helping him.

DISCUSSION

Dr. Fox said that from the clinical appearance he would have made a diagnosis of ringworm. The sharply defined, vesicular borders seemed characteristic of such a condition.

Dr. Fraser said that he was inclined to agree with Dr. Fox that the large lesions on the back resembled tinea. One of these lesions farther down on the back was so suggestive of mycosis that he decided the most probable diagnosis was mycosis fungoides. It was not possible, however, to be dogmatic in such a case, for further observation was required.

Dr. Satenstein said that he had studied the tissue from the case and had noted the typical structure of mycosis.

Dr. Parounagian agreed with Dr. Fox's statement that the lesions were too sharply defined for mycosis fungoides. He favored the diagnosis of tinea circinata, and suggested the application of 5 per cent. chrysarobin in chloroform to one of the patches as a therapeutic test.

Dr. Highman said that he thought the case was obviously one of mycosis, and could not leave unchallenged the clinical diagnosis of ringworm. Certainly there was nothing present to contraindicate mycosis. So far as he had read, the lesions of mycosis fungoides in the prefungoid stage were more likely to be sharply demarcated than otherwise. The almost perfect ringworm shape was not adverse to the diagnosis of mycosis — not that it was common, but it was not uncommon. The mere fact that a lesion was circular, and had a border of vesicles and was scaly, might suggest ringworm, but not every lesion of that type was ringworm. Dermatologists were too much inclined to be like the laity and think that every lesion of the type in question was ringworm. Scaling, lichenification and a certain amount of vesiculation were found in a good many types of mycosis in the early stages.

Dr. Abramowitz said that the patient was under observation for some time at the Gouverneur Hospital Dispensary in the service of Dr. Thornley. The first diagnosis made was generalized tinea, although the patient had not at any time shown any vesicular lesions. Later, he developed a marked eruption on the scalp, with peculiar figurate and gyrate patches with lesions within a lesion. The infiltration and itching became more marked, and this led them to consider mycosis in the prefungoid state. Further, microscopic examinations at the Gouverneur Hospital were negative for tinea, and several other examinations at the Vanderbilt Clinic were also negative for tinea. It was felt that if it was not found with the microscope it would not be found by culture. Roentgen-ray treatments during the past week had relieved the itching, and the lesions were getting paler. Several patients with mycosis fungoides had been observed in this stage, all with lesions in the groins which closely resembled tinea. This patient would be considered as having a case of mycosis fungoides, unless the blood picture showed some other condition. Dr. Abramowitz expressed gratification at having his opinion confirmed by the report of Dr. Satenstein on the skin excised for microscopic examination.

Purpura Annularis Telangiectodes. Presented by Dr. Chargin.

R. V., a man, aged 23, single, a mechanic, born in the United States, had nothing in his former history that seemed to have any bearing on the skin eruption presented. The affection began six months before on both arms. Spots appeared which rapidly increased in number and also in size, and by coalescence produce a network of purpuric eruption. Later, the affection appeared on the legs, and at the time of presentation it was symmetrically distributed on both arms and legs. The eruption, for the most part, was on the inner and anterior aspect of the arms and inner and posterior aspects of the legs. The trunk showed few areas. Although the individual lesions increased by enlargement on the periphery, there was no definite tendency to central clearing. In none of the lesions could atrophy be made out. There was no scaling. Telangiectasiae were present, both at the periphery of the lesions and scattered throughout the affected skin. The eruption could not be pressed out. The older lesions were somewhat pigmented. The color of the eruption varied from brick red to iron-rust color. There was no evidence of infiltration in any of the affected skin. There were no subjective symptoms. The general health of the patient was good. The Wassermann test was negative, and a venereal history was denied. The blood picture was normal.

DISCUSSION

Dr. Wise agreed with the diagnosis.

Dr. Chargin said that he hesitated definitely to present the case as Majocchi's disease, because it lacked some of the essentials of that affection. The history was that the disease developed in spots, and that by the development of new spots which joined with those already present the eruption was produced as seen. He had watched some of the lesions from the outset, and while these slightly enlarged at the periphery, none showed the central clearing, nor was there any evidence of atrophy. In the time that had elapsed since the disease first appeared — six months — one would have expected some atrophy, at least in the older lesions. There was no scaliness of the skin, so often seen in Majocchi's disease. Other elements of that affection were present, however, but the points which have been mentioned seemed to militate

against a definite diagnosis of Majocchi's disease. He hoped to obtain a biopsy which might clear up the diagnosis.

Dr. Bechet inquired whether any one present had had any experience in the treatment of the disease with the quartz lamp. Its beneficial effects in angioma serpiginosum were well known, and it might prove of equal value in Majocchi's disease.

Dr. Chargin said that he had treated some patients with the quartz lamp and had noted some improvement, but that he had not sufficient data on which to make a definite report.

Dr. Andrews said that he had treated two patients with violet rays within the past few months, and they showed gradual slight improvement. He did not, however, think it curative.

Dr. Highman said that in estimating the treatment in Majocchi's disease it must be remembered that in three-fourths of the cases the lesions disappeared spontaneously. This was not so in angioma serpiginosum.

Epithelioma of Penis. Presented by Dr. Chargin.

G. B., aged 66, single, with no occupation, denied a syphilitic infection, and four Wassermann tests taken since the appearance of the lesion had all proved negative. Four years before, the patient had noted a small erosion in the coronary sulcus. Since then, the eroded area had gradually and slowly increased in dimension to the present size. About a year and a half ago, while in Sweden, he had received injections of arsphenamin and ten injections of mercury, without the slightest influence on the lesion. The lesion was about the size of half a dollar and occupied the left aspect of the shaft of the penis, extending over the sulcus to the glans penis for about one-eighth of its size. It was superficial, slightly moist, crusted — especially at the borders — and soft to the touch except at one end where it was slightly firm to the palpating fingers. The border of the ulceration was distinctly polycystic and slightly raised. The lesion was not painful and did not bleed readily, although mechanical removal of the crust produced bleeding. A section of the tissue taken from the lesion proved it to be a squamous cell epithelioma.

Dr. Chargin said the case was interesting and unusual. He had never seen a duplicate, although he had seen a number of the usual type of epithelioma of the penis. The patient said that the lesion started about four years before and developed as related in the history. While abroad, the patient had been carefully studied, evidently from the standpoint of syphilis, receiving treatment without benefit. When seen by Dr. Goldenberg and his staff at the Mount Sinai Hospital Clinic, taking all the facts into consideration, it was considered to be a case of extramammary Paget's disease, and it was rather a surprise when on section it was found to be a squamous cell epithelioma.

A Case for Diagnosis: Monilethrix? Presented by Dr. Howard Fox.

J. H., aged 20, a farmer, born in Germany, an immigrant under examination at Ellis Island, had an affection that had been present as long as he could remember. His parents and six sisters were living and well. No member of his family, according to his statement, presented a similar condition. He had practically no hair on the scalp, eyebrows, eyelids, axillae and pubes. There were a few ascattered downy hairs of normal appearance and a few unerupted or broken off hairs in the mouths of the follicles, like

comedones. On the left parieto-occipital region, there was a marked eruption of discrete, pinhead, follicular keratoses, feeling, on palpation, like a nutmeg grater. A somewhat similar condition was noted in the axillary and pubic regions. A diagnosis of monilethrix was suggested on account of the absence of hairs and on account of the follicular condition which was one of the characteristic features of the disease. The patient appeared to be normally intelligent. He was a robust man of medium size, in apparent good health.

DISCUSSION

Dr. Highman said that he thought the condition looked like ulerythema ophryogenes; that the lesions at the outer extremities of the eyebrows were baldness; and that the obvious relationship with the process at the hair follicles would indicate that it was an extensive variety of that disease.

Dr. Wise agreed with Dr. Highman, and said that it was hazardous to make a diagnosis of monilethrix in a patient in whom the beaded hairs could not be demonstrated, as in this patient who had a congenital alopecia. He referred to the article writen by MacKee and Rosen, who demonstrated the peculiar tortuosity of the hair within the hair follicle. If a section were removed from the scalp of Dr. Fox's patient this change in the hair follicle might be demonstrated and the correct diagnosis established. The patient's lesions resembled ulerythema ophryogenes.

Dr. Wolf said that clinically the patient seemed to have two distinct conditions: first, an alopecia congenita, which was very obvious; and second, a keratosis pilaris, which was developing. Possibly the hair was inclined to generate through the thickened epidermis and might eventually appear. The reason he did not think the condition was monilethrix was that the patient had never had any hair; one primarily had to have a condition of beaded hair present, whereas this patient had never had any hair. In the axillae and on the backs of the fingers, he showed a typical keratosis pilaris.

Dr. Rosen said that he thought the cases reported by Dr. MacKee and himself ten years before were quite different. Every one of the patients had had a certain amount of hair which was stiff and wiry. Examined microscopically, the hairs showed distinct nodes. Dr. Wise's suggestion for the removal of a small section with a hair follicle would help to clear up the diagnosis. The only symptom that was in favor of monilethrix was the keratosis pilaris. He was inclined to agree with the remarks made by Drs. Highman and Wise.

Dr. Howard Fox said that Dr. Rosen, who had studied this disease, had shared his impression in an informal discussion of the case. Dr. Rosen had said that he could make a positive diagnosis by the feeling of the keratotic follicles. The absence of beaded hairs, he admitted, was a weak point in making the diagnosis. If a further opportunity of seeing this patient presented itself, he would remove some of the hairs from the follicles and examine them. Incidentally, the "ringed hairs," about which several members had spoken, referred to another disease. In monilethrix, the hairs showed a beaded appearance.

Hypertrichosis Treated with the Roentgen Ray. Presented by Dr. Parounagian.

Mrs. W., a private patient, 29 years of age, who had superfluous hair for which she had been treated by a physician who employed the roentgen ray

in such cases, stated that her treatment was begun in 1917 and consisted of ten-minute exposures to different areas, every other day for two months; later, she received two treatments a week for about two months; then she received treatments twice a month; afterward, whenever hairs reappeared, she received treatment. She stated that she received these treatments during 1917, 1918, 1919 and in 1924.

She presented a marked atrophy of the skin, with pigmentation and telangiectasiae on the neck and maxillary regions.

DISCUSSION

Dr. Andrews expressed sympathy for the woman. She stated that she had had about fifty exposures, and had had five or six definite erythemas existing over a period of several weeks. He did not think anything of much value could be done for the condition presented, but some efforts should be made to check such practice.

Dr. Scheer told of a similar case seen about a year before at the Mount Sinai Clinic.

Dr. Goodman said that the patient to whom Dr. Scheer had referred had been at the Skin and Cancer Hospital in the service of Dr. C. M. Williams. At one time they had there what appeared to be a mild epidemic of such cases. The patients came from a number of sources; some had been treated by one person and some by another. One of these persons who had advertisements in one of the less particular urban daily papers, professed to have a roentgen-ray machine which would not give the sad results of roentgen-ray dermatitis, even if applied in sufficient dosage to cause the permanent removal of superfluous hairs. This particular man had been identified with other electrical apparatus in the past, as reference to old files of electrotherapeutic journals testified. The patient presented was misguided enough to permit the use of the supposedly modified roentgen ray, and her face showed objective signs of overdosage not so acceptable to the patient as the loss of hair, which was in itself one of the most positive evidences of such overdosage, and preliminary to the others.

Efforts had already been made through the County Medical Society to abate the nuisance, but in vain. The patient could obtain legal redress only through a malpractice suit. One of these patients had had an offer of settlement. Only by education could this distinctly harmful influence be eradicated. It should be common knowledge that the roentgen ray, no matter how applied, if powerful enough to cause permanent loss of superfluous hair is powerful enough to presage undesired sequelae.

Dr. Parounagian said his object in presenting the case was merely to show the result of the treatment and to ask for therapeutic suggestions.

Dr. Satenstein did not agree with Dr. Andrews that nothing could be done to improve the patient's condition. The vessels could be destroyed by electrolysis. After a year's treatment, he had obtained very good results in similar cases. It was tedious, but it could be done. He had seen some cases in which there had been similar telangiectases following attacks of intense erysipelas.

Dr. Andrews replied that he was aware that electrolysis would destroy some of the telangiectases, but it would not prevent others from appearing, and it would not cure the atrophy nor the shrinking of the skin and dryness of which the patient complained, and which would become more manifest as

time went on. The patients complained most of the shriveling of the face. The atrophy of the elastic tissues could not be cured. These people used very soft roentgen rays. The best results had been obtained in Europe with heavily filtered roentgen rays — filtered with 4 mm. of aluminum.

Dr. Feldman told of a method of destroying telangiectasiae which he had observed when he was in Munich. At one of the clinics they used a cautery, the principle of which was that the white heat did not reach the very end. The electrode ended in a spiral from which there was a pointed prolongation. The heat in the spiral was so regulated that the projecting point did not become white hot, but remained apparently cold. There was sufficient heat in the point to coagulate a small vessel, yet not enough to burn. Local anesthesia was produced with a solution of cocain and epinephrin by means of cataphoresis. The solution was applied by means of a sponge electrode attached to the positive pole of a galvanic battery. At first, about 2 milliamperes was applied. Later, when there was a certain amount of anesthesia present, the current was increased to 10 milliamperes. Thus good anesthesia with thorough blanching of the parts was produced, making the vessels stand out prominently on a white background. A light touch with the cautery point caused the vessel to shrivel up, with the formation of a superficial crust which fell off in a few weeks, leaving a normal surface. There was no injury to the skin, but the atrophy and pigmentation remained.

Arsenical Keratoses. Presented by Dr. Rulison.

Miss A. E. B., aged 46, had had typhoid at the age of 12, and no further illness until three years before presentation, when she had primary anemia and was in bed for three months. She had had two blood transfusions, and recovered. She had been given about five dozen hypodermic injections of cacodylate of soda and had taken two bottles of hemaboloids with arsenic. Since last spring, she had had no anemia and was taking no medicine except hydrochloric acid. The lesions on the hands and feet began to appear five months before, new ones appearing from time to time.

Dr. Rulison said the patient had come into the clinic for the first time that afternoon, and he thought it an interesting case, although he was not prepared to defend the diagnosis unequivocally. Three years before, the patient had had a severe attack of pernicious anemia. She had been given two transfusions, and had gradually recovered. The lesions appeared some months ago, first on the palmar surface of the left thumb and then on the dorsum of the hand. One lesion on the little finger of the left hand was somewhat annular and had a rolled, pearly border; several of the lesions were very thick. The diagnosis of keratosis was perhaps questionable, for only two lesions appeared on the palmar surface. Two other diagnoses had been considered — psoriasis and lupus erythematosus — but it seemed unusual that a woman of 46 should have her first attack of psoriasis so late in life; that the lesions should be only on the extremities, and that they should be symmetrical — all four of the extremities being involved. The condition could hardly be lupus erythematosus, for it lacked all the clinical characteristics. It might be due to arsenic taken in small doses over a long period of time.

Familial Xanthoma Tuberosum Multiplex in Two Sisters. Presented by Dr. Walzer for Dr. Lapowski.

W. P., aged 8 years, a schoolgirl, the oldest of three children, had no history of any skin condition, rheumatism, heart, kidney or liver diseases

in the family. The patient had had measles, whooping cough and diphtheria. The condition presented was first noted at 4 years of age; many new lesions appeared later. These lesions were on the front and back of the chest, neck, upper arms, abdomen, and face, and consisted of pinhead to pea-sized nodules, embedded in the skin, some coalescing to form larger lesions. They were slightly elevated, hard and golden yellow. Some were flat, on a level with the skin. They were not painful nor pruritic. There were no lesions visible on the mucous membranes.

Physical examination revealed a slight enlargement of the heart to the left, a systolic blowing murmur at the apex transmitted to the left and over the precordium. The liver was felt two fingers below the costal margin. The urine was normal. The Wassermann test was negative. The blood cholesterin was 315 mg., cholesterin per 100 c.c. of blood.

W. N., aged 7 years, a schoolgirl, sister of W. P., was the second of three children. She had had whooping cough and diphtheria. On the chest and back, there were a few lesions similar to those on the sister. The mother did not know how long they had been present. Examination showed a slight systolic murmur at the apex of the heart. The liver was enlarged to four fingerbreadths below the free margin of the ribs; the tip of the spleen was felt. The urine was normal. The blood cholesterin was 325 mg. per 100 c.c. of blood.

DISCUSSION

DR. HIGHMAN said that he thought the cases merited more study for a diagnosis. Xanthoma tuberosum should be considered first, for the lesions looked suggestive of that condition. The color was a little too brownish perhaps for xanthoma, but this color was sometimes seen. The conditions that seemed against that diagnosis were that the extremities were so free from lesions, and, in the second place, the color. In the third place, the lesions on the older girl were soft and rather flabby, and Recklinghausen's disease should be considered, even though there were no freckles on the body. The fact that there was a hypercholesterinemia would in a great measure speak in favor of xanthoma, but not definitely. The matter could be finally cleared up by means of the microscope, which seemed to have been neglected in the study of this case.

DR. WALZER said that these cases were shown because of their interest from a number of points of view: (1) The occurrence of xanthoma in two children of the same family. (2) The high cholesterin blood content — 315 mg. per 100 c.c. of blood in the older child and 325 mg. in the other. The mother of the two children and the brother — a boy of about 3 years — were also examined. While they showed no xanthoma lesions, their blood cholesterin was 305 mg in the mother and 210 mg. in the boy. (3) Association of cardiac and liver conditions with the xanthomas. It was interesting that both these children presented mitral lesions. Of course they might be rheumatic, but occurring in only these two children with xanthoma lesions, the boy being free, with no rheumatic history either in the children or in the other members of the family, one might suspect that possibly they had xanthoma deposits on the cardiac valves. The liver enlargement in both cases, especially the older one, would also suggest either xanthoma deposits or some form of cirrhosis. (4) Distribution. Why were the lesions only on the body and not on the extremities? Xanthoma lesions have been produced in animals experimentally by feeding the animals with cholesterin and traumatizing the skin, and lesions have occurred on the skin at the point of injury. In these cases, there probably

was no such trauma; but in one with a high cholesterin blood content pruritic conditions of the skin may cause excoriations and the local deposit of cholesterin. Cases have been reported in which they occurred following measles, the xanthoma lesions appearing on areas of the skin previously the sites of the measles rash. However, in these two cases, Dr. Walzer could not account for the distribution.

As to the suggestion that the condition might be Recklinghausen's disease, Dr. Walzer said that by daylight the lesions were a typical golden yellow. There were no pigmentations, no fibromas or neurofibromas and no mental disturbance. These were cases of familial xanthoma, a result of a high cholesterin blood content, most likely congenital—a "cholesterin diathesis."

DR. HIGHMAN said that in discussions on the differential aspects of Recklinghausen's disease, one constantly heard emphasis laid on the absence of mental deterioration as being against the diagnosis of Recklinghausen's disease. In his opinion, it was a myth. He had seen as few people with Recklinghausen's disease lacking mentally as he had seen dermatologists so handicapped. It was probably only the ordinary ratio of mental inferiority that was found in Recklinghausen's disease.

DR. SCHEER said that he had not observed mental deterioration in any of the cases of Recklinghausen's disease that he had seen.

MORPHEA GUTTATA. Presented by DR. CHARGIN.

F. L., a woman, aged 39, married, a housewife, had enjoyed good health except for an attack of encephalitis one year before. She was of the neurotic type. Her skin eruption first appeared about fourteen years before, and since then new lesions had developed from time to time. The eruption was scattered over the entire body except the face and feet. On the arms, the eruption was present in greatest amount on the flexors, there being only two or three lesions on the extensors. On the upper arms, the lesions were mostly on the outer aspect. The greatest number of lesions was on the anterior aspect of the chest and abdomen, with an especially large crop on the breasts. The lesions on the legs were mostly on the flexors. The eruption showed no tendency to group itself around the olecranon or knees. The back showed a considerable number of lesions, but not so many as on the chest or abdomen. The lesions were discrete, only here and there being confluent. There was no definite grouping. The lesions were of two types: (1) round, pinhead to pea-sized, somewhat depressed scars, present for the most part on the upper legs and on the back; (2) pinhead to pea-sized round, either on the level with the normal skin, slightly raised, or somewhat depressed. The base of the lesion was snow-white in appearance, and every one of them showed a narrow telangiectatic border which extended for one-sixteenth inch (1.5 cm.) toward the normal skin. The base of some of the lesions showed peeling, the pellicle being perfectly white. The pellicle could be scratched off without causing bleeding of the underlying surface. The lesions were slightly papular, or even with the surface of the skin. The entire lesion was soft when palpated. The patient stated that the lesions of Type I developed from Type II in the following manner: When Type II lesions were fully developed, some of them became infected spontaneously, and then developed some "pus," eventually ulcerating and leaving scars of Type I. Although the patient had been observed for a period of more than two months, no such developments had been observed. It was possible by force to pick out the floor of lesions of Type II, leaving a slightly bleeding surface, which when healed resulted in lesions of

Type I. The patient exhibited lesions in all stages — what appeared to be very early ones and fully developed ones. There were several linear lesions on the body bearing the characteristics of Type II. There were no subjective symptoms. The Wassermann test was negative. The Pirquet test gave a moderate local reaction, but no focal reaction. Intradermal Old's tuberculin, 1:60 gave a strong local but no focal reaction.

DISCUSSION

DR. WISE agreed with the diagnosis of morphea guttata, although he thought that perhaps other diagnoses might be made. Not every case must necessarily correspond with the technical textbook description. This patient had a distinct scleroderma in spots, with a violaceous band around each spot, and the fact that she had papules on the forearms did not militate against the diagnosis. He had seen that in a case of this type. A microscopic diagnosis would be especially interesting and instructive.

DR. LEVIN said that he had seen the patient a month earlier at Mount Sinai Hospital, and at that time she showed the lesions as presented. They were not atrophic, and were surrounded by small borders almost telangiectatic. At that time he had thought the condition was probably due to tuberculosis, or possibly to syphilis, and it still impressed him as being of the same type.

DR. PAROUNAGIAN agreed with Dr. Levin. He said that if one looked at the forearm lesions, no other diagnosis could be made. The lesions were scaly, with depressed centers. He favored the diagnosis of papulonecrotic tuberculids.

DR. ROSEN said that he thought the case was unusual; he had never before seen one just like it. He did not think it was a case of morphea guttata, and was inclined to favor the diagnosis of some form of tuberculosis — perhaps some form of sarcoid or lupus erythematosus. Some of the lesions suggested atrophic lichen planus. The diagnosis could not be made without further study.

DR. CHARGIN confessed frankly that he did not know what the diagnosis was. The condition was presented as a possible morphea guttata, because, taking everything into consideration, it corresponded more with that condition than with any other. The only points in favor of papulonecrotic tuberculid were that the lesions were somewhat papular and circular, and that the end process resulted in a depressed lesion. On the other hand, against this diagnosis were: (1) the distribution — the lesions being mostly on the trunk, with few lesions in the characteristic tuberculid locations; (2) the duration and seasonal element — the eruption being constantly present in this case, with new lesions developing regardless of season; (3) the age of the patient; (4) the fact that the telangiectasiae present in this case so far as Dr. Chargin knew, were never described in papulonecrotic tuberculid; (5) the snow-white base of the lesions which, so far as he knew, was never observed in papulonecrotic tuberculid; (6) the negative evidence of active tuberculosis, so far as a clinical examination disclosed; (7) the fact that not a single one of the lesions which he had observed developed like a papulonecrotic tuberculid, namely, a deep papule, with eventual softening, crust formation, and scarring. Although of no decisive value, it should be noted that the tuberculin test was negative, so far as a focal reaction was concerned. Concerning lichen albus, he had observed no lesions that in the slightest resembled a lichen planus lesion. Moreover, in the few cases of lichen albus that he had had occasion

to examine, the lesions were grouped and were not so disseminated as in this case. Syphilis could be ruled out by the repeated Wassermann tests. He had been unable to obtain a biopsy, but if successful would report the findings at a later date.

DIFFUSE ATROPHODERMA. Presented by DR. HOWARD FOX.

Previously presented (ARCH. DERMAT. & SYPH. **9**:639 [June] 1924). Since the last presentation, there had been a marked diminution in the area of localized scleroderma, the patches of erythema, atrophy, and pigmentation having remained stationary.

DISCUSSION

DR. BECHET said that the case markedly demonstrated the interesting association of acrodermatitis and scleroderma which was occasionally observed, from time to time, in the same patient. The association of the two conditions was too frequent to be regarded as only coincidental.

DR. WISE agreed with the diagnosis that the condition was a scleroderma that had reached the end stage of atrophy. The pigmentation which Dr. Fox mentioned was a common accompaniment of the disease.

LEPROSY; MACULO-ANESTHETIC TYPE (CASE PREVIOUSLY PRESENTED). Presented from the Vanderbilt Clinic by DR. ABRAMOWITZ.

Mrs. Alice S., colored, aged 33, born in the British West Indies, who had lived for six years in this country, had had an eruption for about two months. On her thighs were quarter dollar sized scaly and slightly infiltrated patches with centers somewhat paler. The upper part of the right arm presented three superficial, serpiginous and scaly lesions that appeared slightly atrophic. All these lesions were definitely anesthetic. The soles were covered with pea-sized pigmented macules. She had had no miscarriages, and her Wassermann test was negative. Two nasal smears, even while she was under treatment with potassium iodid, were negative. A biopsy report had not yet been received. The ulnar nerves were enlarged, and the outer third of the eyebrows was thinned out.

LEPROSY. Presented by DR. CHARGIN.

Y. C., a woman, aged 47, was previously shown at the November, 1921, meeting of the Section as having a typical case of circinate maculo-anesthetic leprosy. She had since been under treatment, receiving injections of the ethyl esters of chaulmoogra oil, with the result that most of the circinate and macular lesions had disappeared, leaving somewhat pigmented and slightly atrophic skin. Sensation had improved, but she was now developing the nodular type of the disease and showed several pea-sized to hazelnut-sized nodules on the posterior aspect of both legs, with similar but smaller lesions on the back and arms.

DISCUSSION OF TWO CASES OF LEPROSY

DR. ABRAMOWITZ, referring to his case, said that it was always difficult to make a diagnosis of the maculo-anesthetic type, especially in the earliest stages; but in good daylight, this woman showed patches which presented the bluish-red tinge on the edge, which were hypo-esthetic lesions. The ulnar nerve was not markedly thickened, but it seemed more so than normal. The outer

end of her eyebrows was thinned out. She came from the British West Indies. Dr. Abramowitz said he had seen several cases from that section during the last six months. Two nasal smears were negative even while she was receiving potassium iodid. He did not claim that the diagnosis was definite, but he did not know what condition this could be other than a very early or mild type of maculo-anesthetic leprosy. Treatment was postponed until a biopsy report was received.

Dr. Chargin said that from a perusal of the literature he had been led to believe that the nodular type of leprosy rarely followed the maculo-anesthetic. The reverse was more common. The case he had presented was therefore an instance of the rarer occurrence, namely, the transformation of the maculo-anesthetic type of leprosy into the nodular variety.

Adenoma Sebaceum (Pringle Type). Presented by Dr. Chargin.

L. B., a young woman, aged 16, a factory worker, American born of foreign parentage, had two sisters, neither of whom was similarly affected. Examination of the mother showed no skin affection. The father exhibited several scattered tumors on the trunk and face, with some patches of pigmentation, and might be considered as having an aborted type of Recklinghausen's disease. The patient suffered from "convulsions" in early childhood, which continued until she was 2 years and 6 months old. Later, she again suffered from "convulsions," but during the last eight years she had been entirely free from any attacks. Until recently she had suffered from severe headaches. Her skin affection was first noted in early childhood. The eruption was located over the center of the face, the largest lesions being noted on the chin and around the nose. The lesions varied in size from that of a pinhead to that of a millet seed. They were reddish and fairly firm to the palpating finger.

Dr. Chargin stated that because of her severe headaches the eyes were examined, and it was found that she had choked disks, 2½ diopters in the right eye, 1½ diopters in the left eye. The examination was made by Dr. Ziporkes. Her vision, however, was normal. Just how long the choked disks had existed, he was unable to say, but since she had been under observation — about five months — no change had been noted, nor had her vision been affected. Dr. Chargin thought that the choked disk was evidence that the patient was suffering from tuberosclerosis, and that she had lesions similar to those on the face pressing on the nerve sheath.

DISCUSSION

Dr. Fox said that he could not agree with Dr. Highman's opinions concerning the mental condition in adenoma sebaceum. He felt that it was a generally recognized and established fact that many patients with adenoma sebaceum showed an inferior mentality. His own experience agreed with the general opinion.

Dr. Gilmour said that many cases were associated with mental deterioration. He had seen a good many such cases in the last fifteen years at Randall's Island.

Recklinghausen's Disease. Presented by Dr. Chargin.

R. S., a man, aged 37, married, a laborer, born in the United States, had been under treatment for syphilitic optic atrophy. Although he denied a

history of syphilitic infection, his Wassermann test proved strongly positive, + + + +. The skin examination showed no manifestations of syphilis but a well developed case of Recklinghausen's disease, presenting all its cutaneous manifestations — tumors, pigmentation, blue spots and hernias of the skin. The entire body was affected, the lesions being particularly numerous on the trunk and less marked on the face and extremities. The tumors varied in size from that of a pea up to that of a walnut, and some of the larger ones were pedunculated. The spots of pigmentation, which were brown, varied in size up to a silver dollar, and the lesions were rather scant. The blue spots were scattered mostly over the trunk. On palpation, many of the blue spots, as well as tumors, presented hernias. The mucous membrane was not involved. The man's mentality seemed to be normal. The patient said that his malady had existed since early childhood, and that his father and grandfather also had had the disease.

LICHEN PLANUS OF THE PENIS. Presented by DR. ABRAMOWITZ.

A. B., aged 27, a salesman, born in the United States, referred by Dr. Batzes, had a condition that began eighteen months before, following intercourse, when the patient noticed an abrasion on the under surface of the penis on the right side, near the frenum. A few days later, the abrasion healed up, leaving a bluish plaque the size of a pea. The lesion then began to spread, producing a continuous line of bluish papules on the shaft and glans, in the form of an oval, the meatus inside of it. A few discrete papules, slightly scaly, also appeared on the shaft of the penis. The condition had remained practically stationary for the past twelve months. A Wassermann test made eighteen months ago was negative; another made three months ago was also negative. The patient had been tested with mercury and arsenic without results.

PAPULONECROTIC TUBERCULID. Presented by DR. CHARGIN.

F. G., a man, aged 26, an office worker, said that he was perfectly well until eight months before. At that time, lesions appeared on the extensors of the forearms. They were small, deep-seated, and later became ulcerated, finally disappearing. As the older lesions disappeared, new ones kept forming, so that at the time of presentation he exhibited scars — small, round, somewhat depressed — the remains of former lesions, and many active small lesions, especially on the backs of the fingers and hands. The active lesions were seen in the various stages of evolution and involution. The patient suffered from cold hands and feet, and there was considerable redness of the hands and feet at the time of presentation.

The patient denied a venereal history, and the Wassermann test proved negative.

LUPUS VULGARIS. Presented by DR. CHARGIN.

J. R., aged 34, married, a barber, born in Italy, was the subject of pulmonary tuberculosis of both upper lobes, the disease being in the moderately advanced stage. It was impossible to ascertain how long he had been suffering from his pulmonary affection. There was no cough, and such sputum as was obtained was negative for tubercle bacilli. The skin trouble began eight years previously. The first patch appeared on the right side of the neck, the other patches appearing later. The last area to be involved was the ear, which had been affected for a year. At the time of presentation, the patient

exhibited two palm-sized and one twenty-five cent piece sized patch on the right side of the neck; one patch, 2 by 2 inches (5 by 5 cm.), on the anterior aspect of the left shoulder; one patch over the right Achilles tendon; one dollar-sized patch under the chin in the hairy region, and an involvement of the entire outer left ear, the infection having spread to the skin in front of and behind this ear. The infiltration was brownish, with serpiginous borders showing numerous nodules; the central portion of the infiltration, especially of the older patches, showed considerable scarring studded with nodules. On the ear, the infiltration was of the tumidus type, the ear being two to three times its normal size. On the lobule of the ear, as well as on the skin in front of and behind the ear, were pea-sized to bean-sized soft and brown infiltrations, isolated and confluent. There was little ulceration, and such as was noted was on the neck lesions. The mucous membrane of the mouth was free from evident lesions. The glands of the neck were enlarged, but isolated, with no evident softening. The Wassermann test proved negative.

HEMANGIO-LYMPHANGIOMA CIRCUMSCRIPTUM. Presented from the Vanderbilt Clinic by DR. ABRAMOWITZ.

Mrs. C. D., aged 40, born in Russia, had a lesion located on the outer side of the left thigh, which was of ten years' duration. It was the size of a silver half dollar, and was made up of pinhead verrucous and angiomatous lesions. Some telangiectases also were present.

GRANULOMA ANNULARE. Presented by DR. WALZER for DR. LAPOWSKI.

S. S., a woman, aged 50, married, who had had five pregnancies and one abortion, fourteen years before had been operated on for removal of one ovary. She had had no other diseases. The condition presented was of about four to five months' duration; according to the patient's story, the lesions appeared almost simultaneously, and were distributed on the dorsum of the left hand near the base of the second, third and fourth fingers, on the outer part of the index finger near the base and in the center of the dorsum of the right thumb. The lesions consisted of a number of ringed or crescentic groups of nodules with smooth surfaces, pinkish white, sharply outlined and shiny. They were deeply seated in the skin and hard. Individual nodules in these rings could be made out easily. The centers of the rings were clean, with normal skin.

LUPUS VULGARIS. Presented by DR. WALZER for DR. LAPOWSKI.

G. J., a schoolboy, aged 9, the third of five children, all apparently healthy, had had generalized "eczema" until 4 years of age, whooping cough at the age of 4, influenza at 5, measles at 6 and influenza at 8 years of age. There was no history of tuberculosis in the family.

About three years before, a bluish lump appeared on the upper left thigh. It soon opened, and ulceration developed. He had had this for about two months before he came to the clinic. He first appeared at the clinic in December, 1922, for a longitudinal tumor-like infiltration on the anterior surface of the upper left thigh. It measured about 2¼ by 1¼ inches (5.6 by 3 cm.). The central part was ulcerated with raised borders. The whole infiltration felt hard, smooth, partly movable and was painless. The ulceration did not extend deeper than the infiltration. No glands were palpable anywhere. The patient was dressed daily at the clinic with ordinary applications and was

given thyroid extract and potassium iodid. After seven weeks of treatment, the lesion gradually healed, and in April, four months after his first appearance, the ulceration, which had at first extended but never beyond the hard infiltration, had gradually healed, leaving a smooth, slightly infiltrated scar.

Two weeks before presentation, after an absence of a year and a half, the patient returned to the clinic with lesions as presented. The mother claimed that these lesions first appeared five months before, about six months after the patient's last attack of influenza, and that these lesions took about four months to heal. New ones, however, had appeared.

The patient presented a white, soft, longitudinal scar, with a slightly pigmented border, on the thigh, the remains of a previous lesion. In the region of the scar were a number of nodules of different appearance, depending on the age of the lesion. They first appeared as hard, millet-sized brownish-red painless papules; on diascopic pressure, brownish pigmentation remained, just above the large scar. They gradually increased to the size of a pea, and then gradually became softer, somewhat flatter, smoother, surmounted with thin scales and without necrosis, and disappeared, leaving pigmented scars. This process, according to the mother's story, took about four months. On the buttocks and elbows, there were a few similar scars, probably the result of similar lesions. Physical examination revealed an apparently healthy boy. A roentgenogram of the chest showed that the right hilus had several foci of calcification, pointing to tuberculous glands. The Wassermann test was negative. Tuberculin tests at different times were negative.

Granuloma Annulare. Presented by Dr. Feldman.

H. E., aged 5, had developed the lesions on her hands about six months before. Two months later, a second crop appeared. When first seen, there was some hyperkeratosis which gave them the appearance of large warts.

Pemphigus. Presented by Dr. Wolf.

Dr. Wolf reported on a case of pemphigus previously presented at the October meeting. The patient had developed new crops of bullae; the old ones had disappeared. It was most probably a case of pemphigus. The patient was still holding his own constitutionally and in appearance. He was receiving coagulen, and roentgen-ray treatment over the suprarenals, fractional deep doses, without any avail so far as preventing new lesions. Dr. Wolf said that he would try to present the patient at the next meeting.

Replying to an inqury from Dr. Goodman as to whether the patient had been receiving arsenic, Dr. Wolf said that he had been taking large doses of arsenic.

Oscar L. Levin, M.D., Secretary.

ST. LOUIS DERMATOLOGICAL SOCIETY

Regular Meetings, Nov. 12 and Dec. 10, 1924

W. H. Mook, M.D., *Presiding*

A Case of Colloid Degeneration of the Skin. Presented by Dr. W. H. Mook.

A blonde woman, aged 17, from the Washington University Dispensary, had had an eruption on the neck for the past two years. Her family history and past history were irrelevant. Recently the lesions had apparently grown

more prominent. Examination at presentation revealed an eruption of discrete and grouped lemon-colored to yellow papular lesions, from pinhead to split-pea size, flat, firm and translucent, encircling the neck. Tiny dilated capillaries on top of a few of the lesions gave them a brownish tinge. There was a suggestion of circinate arrangement in some of the groups, and many of the lesions did not reveal any fluid or gelatinous substance.

DISCUSSION

All concurred in Dr. Mook's diagnosis of colloid degeneration of the skin.

A Case for Diagnosis. Presented by Dr. C. Julian Lunsford.

J. S., a patient from Dr. Engman's Clinic at Barnard Free Skin and Cancer Hospital, aged 58, a houseman, gave a negative family history. His past history revealed an attack of influenza two and one-half years ago, followed by double pneumonia with an abscess of the lung. The present condition began two months ago as pruritus on the inner side of the right ankle, followed by redness and "weeping." The condition spread upward and to the other leg, the trunk and upper extremities being ultimately involved. At presentation, there was observed a red, mottled, papulovesicular eruption with crusting and induration. Some of the papules were discrete; others coalesced. They were most marked on the lower right leg, in the popliteal spaces, particularly on the left side where the epithelium was denuded and on the inner aspects of the thighs where the papules were most numerous. The upper extremities, especially the flexor surface, and the back of the neck showed pinhead sized papular dermatitis. The pruritus was marked.

DISCUSSION

Dr. Richard Kring made a diagnosis of eczema with possibly an infection from pus germs. The eruption on the legs and body he thought was dermatitis medicamentosa.

Dr. Cornbleet said that he thought the spreading lesions were an infectious eczematoid dermatitis of the follicular type, secondary to those on the right ankle.

Drs. Mook, Greiner and Brown concurred in the diagnosis of eczematoid dermatitis, Dr. Mook adding that the infection on the legs had extended over the body as the result of scratching.

A Case for Diagnosis: Herpes Zoster Bilateralis or Herpes Zoster with Aberrant Vesicles. Presented by Dr. Richard S. Weiss.

A man, aged 41, a coal miner, a patient from Dr. Engman's Clinic at Washington University Dispensary, had had pain in the right side of his chest ten days before presentation. Nine days previous to presentation, blisters had appeared on the right side of the chest, and three days later they were observed on the left side of the chest, but at a higher level and extending upward toward the axilla. At presentation, five groups of vesicular lesions were observed on reddened bases on the skin of the right thoracic region, with three similar groups on the left side. The lesions on the right appeared to follow the course of the eighth thoracic intercosal nerve; those on the left following roughly the fifth or sixth intercostal nerve. There was no history of drug ingestion or of any contact with varicella.

DISCUSSION

The consensus of opinion favored a diagnosis of herpes zoster bilateralis, Drs. Greiner and Kring commenting on the fact that it was the first case of bilateral zoster observed by them.

Dr. Mook remarked that the lesions gave the appearance of bilateral herpes zoster with the lesions drying up. He felt that the lesion on one side, diagnosed without question as herpes zoster, had followed the typical course of the disease.

Dr. Weiss closed the discussion by adding that in his mind there was still some doubt as to the bilateral nature of the eruption. The lesions on the left side of the thorax did not seem to follow the distribution of one nerve, whereas those on the left side did follow such a regular course, giving the impression that it might be a case of herpes zoster with aberrant vesicles. He described a case of true herpes zoster bilateralis in a man who had typical lesions around the neck and shoulder.

A Case of Lichen Planus in a 9-Year Old Boy. Presented by Dr. Richard S. Weiss.

A boy, from Dr. Engman's Clinic at Washington University Dispensary, had had the present eruption for approximately one year. New lesions had appeared from time to time. The eruption was symmetrical and the involvement general, with the exception of the face, palms and soles. The lesions consisted of flat, angular, violaceous papules, many covered with fine scales, and others with minute, scarlike depressions. Some of the lesions had coalesced, forming patches. Pruritus was rarely noted. The Wassermann reaction was negative. A biopsy showed the presence of acanthosis and parakeratosis with subpapillary round cell infiltration of the upper corium, which, however, was not dense. Only moderate improvement resulted from arsenic and mercury medication.

DISCUSSION

Dr. Kring said that he thought it was a case of lichen scrofulosorum, judging from the picture presented.

Dr. Cornbleet remarked that the scarring suggested a tuberculid.

Dr. Greiner stated that the history of the case with the changing lesions, some appearing, others disappearing, might possibly indicate parapsoriasis, in which opinion Dr. Brown concurred.

Dr. Weiss said that the boy had been in the St. Louis Children's Hospital for a number of weeks. Careful examination revealed the presence of no other disease, but there were the same lesions as seen at this time, not quite so profuse, but typical angular lesions closely resembling the violaceous papules of lichen planus, the rings being composed of shiny, angular, violaceous papules. The boy improved somewhat on mercury medication, and at this time showed marked improvement over the condition presented several weeks before.

Dr. Conrad said that he also thought the condition was parapsoriasis rather than lichen planus. He could not see any angular outlines, or the violaceous, flat papules referred to by Dr. Weiss. The lesions presented a definite scaliness at this time.

Dr. R. H. Davis also diagnosed the eruption as parapsoriasis. He recalled a case which he had seen in the Barnard Free Skin and Cancer Hospital some

years ago, which passed through stages so closely resembling lichen planus that there seemed no doubt as to the diagnosis, until later developments revealed a frank case of parapsoriasis.

Dr. Brockelmann also favored a diagnosis of parapsoriasis of the lichenoid type.

Dr. Weiss again referred to the biopsy findings which showed parakeratosis, acanthosis and subpapillary infiltration of the small round cells, which, although not typical of lichen planus, did definitely resemble those lesions.

Dr. Mook's diagnosis was parapsoriasis, judging from the history of the case, the characteristic lesions which were distributed over the body, the arms and forearms being almost entirely free, and the condition yielding to no medication. He felt that these symptoms in this case were characteristic of parapsoriasis.

A Case for Diagnosis. Presented by Dr. C. Julian Lunsford.

F. W., aged 39, a machinist, a patient from Dr. Engman's Clinic at the Barnard Free Skin and Cancer Hospital, complained of lesions over the left tuberosity of the sacrum composed of small papulovesicles which were more or less grouped, accompanied by intense pruritus, which was aggravated at night time. The eruption had been present intermittently since August, 1924, with periods of remission of three or four weeks' duration. At presentation, red, moderately infiltrated patches were noted, which gradually merged into normal skin. Each patch was studded with numerous small maculopapules, some of which showed circinate grouping, the patches varying in size from that of a split pea to that of a half dollar. The redness partially faded on pressure. There had been continuous pain for several days, accompanied by pruritus, which was greatly aggravated at night.

DISCUSSION

Drs. Greiner and Brockelmann felt that the condition was recurrent herpes zoster, more pronounced in the two upper lesions, which showed dried-up vesicles in groups.

Dr. Brown, on first observation suspected syphilis, but after hearing the history of the case, he favored a tentative diagnosis of herpes zoster.

Dr. Conrad felt that the diagnosis lay between herpes zoster and late syphilis, the upper lesions with the small vesicles containing infiltration suggesting syphilitic lesions.

Dr. Davis said that he thought the symptoms of pain, pruritus and the tendency to recur were contrary to a diagnosis of syphilis, although the upper lesions were slightly indurated. He thought the condition was more probably recurrent herpes.

Dr. Kimbrough agreed with Dr. Davis that the changes in the lesions, together with the symptoms of pain and pruritus were opposed to a diagnosis of syphilis, being more suggestive of recurrent herpes zoster.

Dr. Mook stated that the recurrence of the lesions in groups of vesicles with burning and itching sensations led him to believe that the condition was recurrent herpes. He accounted for the infiltration by the numerous relapses at the same site, which had kept the skin in a state of constant irritation causing chronic inflammation, however without any infection.

A Case of Late Syphilis. Presented by Dr. C. Julian Lunsford.

A. R., a patient from Dr. Engman's Clinic at the Barnard Free Skin and Cancer Hospital, aged 38, a housewife, married, with four normal, healthy children, gave a history of miscarriage at three months during the last pregnancy. Two years before, following trauma, painless nodules were observed on the right knee and on the upper portion of the right leg. They were at first subcutaneous. Later some of them broke down into ulcers. There was no history of pruritus. At presentation, a lesion the size of the palm was seen, composed both of tubercles and ulcers, the former purplish, indurated and having a granulomatous feel; the latter, with a punched-out appearance. The tubercles, some discrete, others conglomerate, were most numerous at the periphery of the lesion, the border of which was serpiginous.

DISCUSSION

It was the consensus of opinion that this was a case of late syphilis.

A Case of Maculo-Anesthetic Leprosy. Presented by Dr. C. J. Lunsford.

A patient from Dr. Engman's Clinic at the Barnard Free Skin and Cancer Hospital, had migrated to the United States from Mexico, two years before presentation. He could give no history of contact with other lepers. Trauma of the right elbow two years before was followed by partial paralysis of the right hand, which lasted for several months. In July, 1924, the patient noticed a lesion on the right eyebrow, which was soon followed by similar lesions on the face, elbows, ankles and other parts of the extremities and trunk, in the order named. These were accompanied by subjective sensations of the various paresthesias, and occasionally by darting pains of the right elbow and hand and both feet. The right hand had occasionally been edematous, with weak muscle power. There were no bullous eruptions and no constitutional or prodromal symptoms. Eight weeks before, the patient developed a lesion on the foreskin dorsal to and running parallel with the sulcus back of the corona. At presentation, numerous maculopapular lesions were observed on the areas named, varying in size from that of a split pea to twice the size of the hand, generalized, more or less symmetrical, with raised red borders and faded fawn-colored centers. The centers had fine gray scales, and were completely anesthetic as contrasted with the partially anesthetic borders. The small lesions were round or oval; and the large ones were irregular with serpiginous, gyrate borders. The Wassermann reaction was three plus in cholesterin antigen. The nasal smears, tissue juice smears and the biopsies, repeated several times, were negative for acid-fast bacillus.

DISCUSSION

Dr. Mook called attention to a peculiarity in this case: the skin eruption dating back a full year, the primary lesion on the genital organs dating back eight weeks and the Wassermann reaction being three plus. There was marked anesthesia.

A Case of (Generalized) Lichen Planus. Presented by Dr. W. H. Mook.

H. B., aged 21, had always enjoyed good health until about six weeks before presentation, when he noticed a red eruption on the hips, which spread rapidly over his entire body with the exception of the face. It did, however, appear on the mucocutaneous surface of the lips. The case was presented

because of the fact that it was the most diffuse case of lichen planus ever observed by Dr. Mook, the face and scalp being the only areas not involved. The palms were covered in their entirety with a thickened, papular, horny eruption. The plantar surfaces of the feet were in exactly the same condition. The mucous surface of the cheeks was covered with linear, papular, circinate, typical lesions of lichen planus. The tongue had a few white streaks, as occasionally seen in leukoplakia, but the entire surface was studded with yellowish-gray papular lesions somewhat like those on the palms, but not so infiltrated. The eruption developed over the entire body within six weeks. The patient was given injections of mercuric chlorid, beginning October 6, and improvement was marked. He had no constitutional symptoms such as usually accompany generalized cases.

DISCUSSION

Drs. Kring and Brown said that they thought the condition was generalized lichen planus, Dr. Brown remarking its presence in the mouth and on the hand.

Dr. Greiner said that the presence of the lesions on the hand and on the tongue was most unusual. He thought it was the most generalized case of lichen planus which he had ever observed.

Dr. Conrad stated that he had a patient under treatment for lichen planus who had profuse lesions on the body, but as he had never seen lesions on the palms, the dorsa of the hands and the neck reaching up to the ears, he had been inclined to doubt the presence of lesions of lichen planus at those sites. Pressure around the collar line in the patient presented seemed to give a well marked line of lesions.

Dr. Davis said it was the most remarkable case of lichen planus which he had ever seen, and the only case with lesions on the palms or soles, or with such extensive lesions on the tongue.

Dr. Brockelmann thought it was a case of acute miliary lichen planus.

Dr. Mook called attention to the most unusual features presented: (1) The papular lesions on the tongue that resembled those on the palms, of a yellowish tinge or fawn-colored gray. The most recent lesions occurred on the floor of the mouth, in the mucocutaneous surface. The palms and soles were involved in their entirety. (2) The absence of constitutional symptoms, even slight symptoms of nervousness.

A Case for Diagnosis. Presented by Dr. C. Julian Lunsford.

Mrs. A. R., from Dr. Engman's Clinic at the Barnard Free Skin and Cancer Hospital, aged 22, gave a negative family history. Two months before presentation, she gave birth to a healthy child. The present illness began five years before with lesions over the sternum resembling "pimples," which did not heal. One over the left clavicle began as a "boil." Similar lesions over the shoulders had no history, except for a gradual development to their present condition. Pruritus was the only subjective symptom. At presentation, there were ten lesions over the sternum, one over the left clavicle and several over both shoulders, ranging in size from that of a split pea to that of a nickel. Two had coalesced. Others were sharply circumscribed, raised, indurated, with an elastic feel. They were red or pink, with shiny tops. Several had enlarged capillaries coursing over them. On the middle of the abdomen, 3 inches (7.6 cm.) above the umbilicus, were six circumscribed, slightly indurated,

slightly scaly lesions, varying in size from that of a dime to that of a dollar, mottled pink or red to normal skin color, the color fading toward the periphery. They were round or oval. Embracing the umbilicus in its extent was a similar lesion, also one under each breast. Just anterior to the axillary fold was a similar oval lesion, and just posterior to the posterior right axillary fold were two oval lesions. There was no history of pruritus or moisture. These lesions had been present since confinement. There was no history of the application of hot water bottles or any other external application at that time or subsequently.

DISCUSSION

DR. KRING said that he thought the lesion on the sternum was a keloid. The lesions on the right side were typical pityriasis rosea. Those in the fold showed inflammation, probably due to some local treatment.

DR. CORNBLEET said that he also thought the lesions on the upper chest were a keloid. There was one typical of pityriasis rosea on the abdomen; also three or four in the lumbar region. The larger aberrant lesions on the anterior abdomen corresponded in color and appearance, except that they were larger than the typical lesions of pityriasis rosea.

DR. GREINER agreed with the diagnosis of acne keloid, but would not venture a diagnosis of the other lesions, which might be due to drug dermatitis of some type.

DR. CONRAD also agreed with the diagnosis of the lesions on the chest, but was reticent in regard to a diagnosis of the lesions on the abdominal wall, which to him appeared larger than those of pityriasis rosea. The lesion under the right breast he thought characteristic of pityriasis rosea.

DR. BROWN agreed with Drs. Kring and Cornbleet.

DR. KIMBROUGH stated that he had seen the case when it was first presented in the clinic. At that time, the lesions did not resemble those of pityriasis rosea, with the exception of one on the back, but rather suggested some chemical irritation. The lesion on the fold seemed to be undergoing a change or evolution of some sort, which to his mind did not seem to indicate a keloid.

DR. DAVIS said that he thought the lesions on the chest were acne keloid. When he first saw the case, he did not think of a diagnosis of pityriasis rosea for the other lesions, but at this time he thought it was an atypical case, the inflammatory character of the lesions being due to the application of iodex.

DR. MOOK agreed that the lesions on the chest and back were sebaceous, cystic lesions, which had later become keloids. The other lesions, however, began as oval or round red plaques, with slight scaling. They were of the same color — not fawn color in the center — and did not have an erythematous ring as seen in pityriasis rosea. Those on the abdomen which seemed to be irritated were distinctly infiltrated, with a rather intermittent infiltration instead of a diffuse infiltration throughout the whole patch. They appeared exactly like the lesions following the ingestion of phenolphthalein, being dark yellow, due, not to any external cause, but to internal administration. Dr. Mook said that he had found it advisable to make no external application in such cases. Keloids, however, will yield to roentgen-ray treatment.

A CASE FOR DIAGNOSIS. Presented by DR. A. H. CONRAD.

Mrs. W., from Dr. Engman's Clinic at the Barnard Free Skin and Cancer Hospital, presented herself in the Clinic on Nov. 28, 1924, for treatment of a papulovesicular, erythematous eruption of the forehead, cheeks, the entire

circumference of the neck, the upper anterior chest and the flexor surface of both arms. In addition, both cheeks were edematous, particularly the right cheek, and were covered with thick yellow crusts, as was the anterior surface of the right ear. There was little pruritus. The entire eruption had developed during the last three days. She had previously been treated in the Clinic for sensitization eczema, being found slightly sensitive to milk and wheat, but she had had no recurrence of this condition from July, 1924, to November, 1924. The previous eruption as well as the present eruption occurred during the latter part of pregnancy.

DISCUSSION

The consensus of opinion favored a diagnosis of sensitization dermatitis.

Index to Current Literature

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